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HYPOCHONDRIASIS.[1]

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HYPOCHONDRIASIS, as a nosological entity, has been long out of fashion. This is curious, since hypochondriacal symptoms are in fact the most common symptoms of mental disorder; they occur alone or with other symptoms, in mild and severe, acute and chronic disturbances. How so omnipresent a clinical fact has reached its current position of disregard is worthy of inquiry. To by-pass the large question of psychiatric classification and the validity of current diagnostic categories, the field of this paper must be restricted; accordingly, the significance of hypochondriasis in what many take to be distinct syndromes, such as involutional melancholia, will not be examined, nor will its occurrence in the various organic disorders.

While hypochondriasis is often used in the vague sense of a general fear of illness, it has a more precise meaning. R. D. Gillespie (1929) defined what he called "the syndrome of hypochondria" as follows:

> A mental preoccupation with a real or suppositious physical or mental disorder, a discrepancy between the degree of preoccupation and the grounds for it, so that the former is far in excess of what is justified, and an affective condition best described as interest with conviction and consequent concern, and with an indifference to the opinion of the environment, including irresponsiveness to persuasion . . . it shades off into schizophrenia . . . in its mild form it is often erroneously diagnosed as anxiety neurosis or hysteria.

The concept of hypochondriasis is of great antiquity and the literature correspondingly vast. Yet the basic notions formulated by the Hippocratic and later Greek schools, invested with the authority of Galen, remained essentially unchallenged up till the seventeenth century. The condition was attributed to disturbances in the viscera behind the xiphoid cartilage and below the diaphragm; Galen believed it was mainly due to the effects of black bile. It was the equivalent in men of hysteria in women. Thus Aretæus, writing on "hysterical suffocation" in the second century, epitomized a view which held currency for a further fifteen hundred years:

> In the middle of the flanks of women lies the womb, a female viscus, closely resembling an animal; for it is moved of itself hither and thither in the flanks, also upward in a direct line . . . and also obliquely to the right and left . . . in a word it is altogether erratic. It delights also in fragrant smells and advances towards them; and it has an aversion to fœtid smells, and flees from them.

[1] The substance of a paper read at a meeting of the New South Wales Branch of the Australasian Association of Psychiatrists on March 23, 1959, at Broughton Hall Psychiatric Clinic.

Large sections of the mediæval and Renaissance pharmacopœia were devoted to various concoctions to be applied at one or other orifice to attract or drive the wandering uterus back to its proper place.

By the late seventeenth century it had been realized that in many ways the hysteria of females was identical with the hypochondriasis of males. Sydenham (1682) had no doubt: hysteria occurred "in such male subjects as lead a sedentary or studious life and grow pale over their books and papers . . . however much antiquity may have laid the blame of hysteria upon the uterus, hypochondriasis . . . is as like it as one egg is to another". Blackmore (1725) remarked that "the Symptoms that disturb the Operations of the Mind and Imagination in Hysterick Women, are the same with those in Hypochondriacal Men, with some inconsiderable Variety". Feuchtersleben (1845) was unambiguous: "Hysteria, the sister condition of Hypochondria, whatever nice distinctions may be between them, is only the same disturbance of the coenœsthesis, as modified in the female sex." Griesinger (1861) expressed the same view. Yet Freud appears to have thought that Charcot had "discovered" hysteria in men, and following Charcot, elevated hysteria again to a diagnostic entity, separating it from its centuries-old association with hypochondriasis.

Galen's pathology of hypochondriasis, after 1500 years of variation on his basic theme, culminated, by the seventeenth century, in that refinement of the humoral pathology which attributed the disturbance to disorders of the spleen, the vapours and perturbations of the animal spirits. Burton (1621), whose famous *Anatomy of Melancholy* remains a monument to his own hypochondriasis, quotes ancient and mediæval authors in the Galenical tradition, but himself pronounces: "Most commonly fear, grief, and some sudden commotion or perturbations of the mind, begin it, in such bodies especially as are ill disposed." In this he was ahead of his time, for the great Thomas Willis in 1667, while admitting hypochondriasis as a disorder of the nervous system, still held its ultimate cause to be impurity of the splenic blood. Sydenham (1682) was, as usual, enlightened and dogmatic: "Hypochondriasis is not referable to any material source." In 1725, Blackmore, writing "Of the Spleen and the Vapours: or Hypochondriacal and Hysterical Affections", anticipated later eighteenth century opinion in declaring that they were "nothing but the Effect of Fantasy, and a delusive Imagination". The view that hypochondriasis was a mental or nervous disorder gained ground in the work of such men as Flemying (1740), Whytt (1764) and Cullen (1777). The point was still being argued in the early nineteenth century by Pinel (1801), Georget (1819) and Esquirol (1820), but the question was generally considered decided by Falret's "*De l'hypochondrie et du suicide*" (1822). Paradoxically, it was for Freud to return to a neo-humoral pathology of hypochondriasis, when he declared it to be a variety of "actual-neurosis", due to the effects of undischarged libido and "without signification in the mind" (Freud, 1917). How he arrived at this anachronistic position we will discuss later.

Over the centuries, many had remarked that preoccupation with and concern over the function of body and mind regularly, if not invariably, precede and accompany severe mental illness. As Robinson (1729) observed:

> Madness and Lunacy are only the Spleen and Vapours improv'd, in different Constitutions . . . it necessarily follows, that they must arise from the same causes, more highly advanc'd into the Habit, which render all the symptoms more dejecting in the melancholy Madness, and the more bold, furious and violent, in Lunacy, or the maniacal Madness.

Arnold's (1806) statement that hypochondriasis "lays a foundation for every species of insanity" was elaborated by Griesinger (1861):

> The hypochondriacal states represent the mildest, most moderate form of insanity. . . . While they, of course, share with the others the generic character of dejection, sadness, depression of mind, diminution of the activity of the will and a delirium which corresponds to this mental disposition, they yet differ from them in this characteristic manner—that in these states the emotional depression proceeds from a strong *feeling* of BODILY *illness* which constantly keeps the attention of the patient concentrated upon itself; that, consequently, the false opinions relate almost exclusively to the *state* of *health* of the subject, and the delirium turns constantly upon apprehensions of some grave malady—upon unfounded and curious ideas regarding the nature, the form, and the danger of this his disease. This feeling of bodily illness is sometimes general and vague, sometimes it resolves into particular anomalous and disconnected sensations . . . one cannot help being struck with the remarkable similarity between this process and the production of hallucinations in general . . . the higher degrees of hypochondria . . . gradually pass, partly through increase of the feeling of anxiety, partly through the fixing of certain attempts at explanation, not only into true melancholia, but even complicated with delusions (ideas of being surrounded by an invisible agency, of being the victim of machinations, influenced by magnetism, etc.). That considerable degree of self-control also which hypochondriacs still possess often disappears during each exacerbation. Could the physicians only observe these paroxysms as freely as they can at any time in severe cases in Asylums, all doubts concerning the mentally morbid nature of hypochondriasis would very soon disappear.

Sir William Gull (1868), like other distinguished physicians of the later nineteenth century, wrote on hypochondriasis. He believed hypochondriacs could be distinguished from the truly melancholic:

> But it may here be remarked that the heightened self-feeling of hypochondriasis does not partake of the despondency of true melancholia, still less of the character of other forms of insane egotism. The patient . . . though depressed in mind, not only wishes to get rid of his malady, but has great faith that he shall do so; a faith which suffers repeated shocks, indeed, from the non-success of particular remedies, but quickly revives in favour of some new mode of treatment.

How, then, did hypochondriasis, somewhere around the turn of the century, come to be relegated to a position of relatively slight importance in psychiatric nosology? In part it had to do with Kraepelin's revolutionary grouping together of all psychotic conditions in the two main divisions of dementia præcox and manic-depressive insanity, and the subsequent revision of this concept by Bleuler under the influence of psycho-analytical ideas. But more important in leading to this gradual neglect of hypochondriasis was the influence of psycho-analytical theory, especially on the question of neurosis and psychosis. There was little argument that severe and chronic hypochondriasis represented one variety of schizophrenia. In his original monograph on schizophrenia, Bleuler (1911) stated: "Most incurable Hypochondriacs are Schizophrenics whose delusions are primarily concerned with their own bodies." Regularly since then, various authors have been led to describe subgroups of schizophrenia which emphasized hypochondriacal symptomatology. Claude (1937), for example, described a "schizoneurotic" variety; Kleist (1941), in his vast list of supposedly distinct schizophrenic states, has one labelled "progressive somato-psychotic"; and the "pseudoneurotic schizophrenia" of Hoch and Polatin (1949) has attained a certain currency. Lewis (1950) notes the regular occurrence in schizophrenics of "curious somatic hallucinations, indicative of morbid attitudes both physiogenic and psychogenic towards parts of the body—queer sexual feelings or distortions and impossible growth of various organs, may be reported. They are usually bound up, as any schizophrenic symptom is likely to be, with delusional and emotional components, which are partly derived from the patient's experiences and psychological development". Ey (1955) states that "hypochondriacal themes . . . constitute the most frequent primary delusional experience at the beginning of schizophrenia". Meares (1959), discussing the early indications of schizophrenia, makes the following statement:

> Somatic symptoms may have a delusional quality which can escape the most astute physician. In fully

> developed schizophrenia, they may have a bizarre quality which makes them easily recognizable as delusions. But in the prepsychotic stage there may be nothing unusual about the symptom itself: the diagnosis rests on the meaning of the symptom to the patient.

Thus the more severe grades of hypochondriasis are, in the general view, subsumed under the heading of schizophrenia, and the question of their nature, course and ætiology becomes one with that of schizophrenia.

But what of the mild and early forms of hypochondriasis? To attempt an answer will involve a slight digression into the question of "neurosis" and "psychosis".

Lewis (1950) has written in unequivocal terms, "the distinction between neuroses and psychoses is at times convenient, but without substance"; but the general acceptance of this fact and its implications is yet to seek. Neurosis, a term used by Romberg (1840-1846) to describe organic disease of the nervous system, is today synonymous with psychogenic illness. Psychosis, a term introduced by von Feuchtersleben (1845) to differentiate primary disease of mind from mental symptoms consequent on organic brain disease, is today taken to mean mental illness, supposed by many to be the outward sign of an as yet undiscovered brain disorder and primarily to be distinguished from neurosis by impaired "reality-testing". For at the time when Freud was demonstrating that the erstwhile organic "neuroses" were diseases of mind—psychoses in Feuchtersleben's sense—Kraepelin was grouping dementia præcox, the major mental as opposed to neurological illness, with thyroid disease and general paralysis of the insane, as a metabolic or degenerative disease of the nervous system. Freud used psychosis for those illnesses in which the patient was grossly disturbed in his relation to the outside world—that is, obviously insane. Such patients were not amenable to the classical psychoanalytical technique (Freud, 1917). Thus it came about that neuroses, the milder disturbances and erstwhile diseases of nerves, were considered to originate in the mind and be amenable to psychological treatment, while psychoses, the original mind diseases proper, were believed not to be amenable to psychological treatment because patients could not be psychoanalysed. As psychoanalysis became the most widely known psychological theory and therefore therapy, it came generally to be believed that patients not amenable to psychoanalysis were beyond psychological understanding and help. Thus the difficulty of explaining severe mental illness on the lines of the libido theory and classical Freudian conflict encouraged the belief that there were two fundamentally different groups of mental illness. Psychoanalysis, indeed, now invests the ego function of reality-testing with such importance that it is considered the main psychoanalytical contribution to the theory of severe mental illness (Glover, 1949):

> The most valuable psychoanalytic contribution to the theory of the psychoses is that concerning the nature of normal reality-function. By far the most reliable indication of psychotic disorder is disturbance of the function of reality-proving: and . . . this disturbance is a measure of the degree of abandonment of objects. We are therefore in a position to indicate the function of reality-proving in terms of the relation of the ego to the objects of its instincts.

Yet if such statements are stripped of jargon, they reduce themselves simply to the old asylum-wall distinction between the sane and the insane. But such a major division is untenable; clinical experience constantly contradicts it. The symptoms of milder mental illness almost always precede or accompany the severer forms, and alienation from external reality is almost always a development from disturbance of inner reality sense. Further, such a division does not allow for earlier, milder and incipient forms as precursors of severe mental illness, and thus prejudices study of the natural history of mental illness from its mildest to its most severe manifestations. As Sir William Gull wrote in 1872, "We require a history and not a definition of disease."

Now what did Freud make of hypochondriasis? Following Charcot, he elevated hysteria again into a diagnostic entity with a specific psychopathology, and made it the paradigm of psychogenesis. Disturbed interpersonal relations originating at the Œdipal level and reproduced in the transference situation were held responsible for "hysteria". But patients with similar somatic symptoms, in whom an Œdipus complex could not be discovered, or who did not respond to the classical technique, were grouped together as suffering from "actual-neuroses"—which included hypochondriasis. In 1917 he wrote:

> Not merely are they manifested principally in the body, as also happens, for instance with hysterical symptoms, but they are in themselves purely and simply physical processes; they arise without any of the complicated mental mechanisms we have been learning about . . . [they] represent the direct somatic consequences of sexual disturbances.

As late as 1925 he wrote:

> From a clinical standpoint the actual neuroses must necessarily be put alongside the intoxications and such disorders as Graves's disease. These are conditions arising from an excess or a relative lack of certain highly active substances, whether produced inside the body or introduced into it from outside—in short, they are disturbances of the chemistry of the body, toxic conditions.

So because hypochondriasis was not explicable in terms of interpersonal relationships traceable to the vicissitudes of instinctual drives, Freud could not see its psychiatric or psychological significance: "The symptoms of an actual neurosis have no 'meaning', no significance in the mind". (Freud, 1917.) This remains the orthodox psychoanalytical position according to Fenichel (1945)—"Hypochondriasis is an organ neurosis whose physiological factor is still unknown . . . it is often combined with acute anxiety neuroses or neurasthenia"—whatever these terms may mean. Thus Freud was forced to board out hypochondriasis from psychoanalysis and to postulate an organic disorder reminiscent of the humoral pathology of the Middle Ages.

Is there an alternative? The problem has been reexamined in a series of papers and monographs over the last eight years by Ida Macalpine and R. A. Hunter. They do not propound a system or a theory of mental structure or function. Rather they emphasize a return to unprejudiced clinical observation of patients, in the light of the basic advances made by Freud: his description and delineation of unconscious mental mechanisms through the revolutionary techniques of free-association, dream and transference analysis—the greatest, perhaps the only methodological, advance in psychology since Aristotle. This, as distinct from the theoretical superstructure and techniques of orthodox psychoanalysis.

Macalpine and Hunter point out that it is widely believed that in medical and surgical practice, patients present with aches, pains and dysfunctions of all kinds, while in psychiatric practice patients present with mental symptoms. Yet this is by no means so. A high proportion of patients attending out-patient departments of all specialities suffer from somatic symptoms which have no physical basis, and many, if not most, psychiatric patients complain at one time or other of symptoms which they refer to their bodies. For psychiatrists, study of somatic symptoms should therefore be at least of the same interest as that of mental symptoms. As hypochondriasis, they are almost invariable precursors and concomitants of mental illness of all degrees of severity, frequently the only manifestations, and lately have been segregated under the label of "psychosomatic". Yet they tend to be neglected in favour of the more dramatic, more easily understood and perhaps less disturbing mental symptoms.

Space forbids an attempt to detail the innumerable complaints which patients may present and the infinite variability of clinical pictures. However, Macalpine and Hunter suggest that it is convenient to distinguish four stages of severity. In the earliest, the patient may complain only of abdominal symptoms, indigestion, nausea, constipation and so on, appearing to all intents and purposes mentally normal. Alternatively, somatic symptoms may not be volunteered unless specifically inquired for, and the patient may complain only of anxiety,

insomnia, inability to concentrate or depression, or of not being himself.

In the next stage, patients localise their altered sensations more precisely. They speak of feeling "as if" something was stuck in their throat, for instance, moving about in their stomach, or crawling on their skin.

After a time, patients may pass into a third stage, when they take their altered sensations more seriously and "as if" becomes a certainty. No longer concerned that they may develop or have a certain disease—as, for instance, cancer, syphilis, tuberculosis or, more lately, "infantile paralysis"—they are now convinced that they have it. At this stage, no longer amenable to reassurance and objective evidence, patients may go from doctor to doctor in quest of confirmation of their body delusions and hallucinations. They become irritable, suspicious, depressed, feel aggrieved, wronged or persecuted, and may misinterpret what is said, as well as actual events.

This stage may pass imperceptibly into a fourth, when delusions and hallucinations no longer remain confined to the body, but become related to the outside world. Patients now develop ideas of reference and influence, ascribing their altered body sensations to external agencies—poison, rays and so on. Such individuals are now patently "mad"—alienated from external reality.

Though reference has been made mainly to a patient's altered relation to his body, many mental symptoms can also be understood in terms of his altered relation to his mind—a distinction perhaps indicated by Burton's recognition of the essential similarity of "the hypochondriacal or windy melancholy" to what he called "head-melancholy". Patients complain that they cannot think properly, cannot concentrate or remember, that they are obsessed by recurring thoughts or ideas or have compulsively to perform certain acts; they may fear that their brain "may snap", or that they will lose control of their nerves or mind.

What of the psychopathology of these disturbances? Macalpine and Hunter emphasize that they are not propounding a general theory, and they prefer not to use the psychoanalytical topographical terms with all their implied assumptions as to the structure of the mental apparatus. But they hold—and unprejudiced clinical observation supports this viewpoint—that hypochondriasis is not explicable either as the outcome of maladaptation to environment, or as psychoneurotic resolution of conflict through the use of mature mental mechanisms.

They consider that the early "psychosomatic" symptoms are traceable to a recent reality stimulus, the significance of which is not consciously apparent to the patient; that this leads to the activation of normally unconscious fantasies and associated emotions, which achieve rudimentary, disguised somatic expression in the symptom. The emotion achieves only partial expression, so that instead of leading to action and thus subsiding, it persists in the guise of the symptom. Such symptoms are therefore not defence mechanisms of the mature mind, but more primitive phenomena, being characterized by a partial break-through and persistence of an unconscious emotion or fantasy. They are not caused by a need for symbolic dramatization of conflict, but are direct expressions of the primitive body-mind unit.

Space prevents a discussion of the nature of these fantasies, but they are essentially concerned with primitive beliefs, wishes and fears concerning the functioning and structure of the body and mind, relating especially to such subjects as sexual identity and procreational possibilities.

What of therapy? In the earlier stages, such patients are usually diagnosed as suffering from anxiety neurosis or hysteria and are generally acknowledged to be accessible to psychotherapy. While a patient's disturbance is confined to his relation to himself, he is by this very fact diagnosed as neurotic, although degree of alienation is no guide to severity of illness. Alienation is a criterion only of the degree of social incapacity or disturbance caused by the illness, but is often mistakenly taken to indicate the psychiatric distinction of a worse prognosis and the necessity of more "radical" treatment. That this is by no means so, is illustrated by the fact that ever since psychiatric statistics were first kept in the eighteenth century, two-thirds of mental hospital patients have recovered with or without treatment. But many patients who are not alienated continue more or less incapacitated throughout life.

In the later stages, there is every reason to think that patients can also be helped psychotherapeutically, provided they are understood. To study mental illness as a continuum from the most mild to the most severe may well provide the basis for such an understanding. Hence Macalpine and Hunter believe that diagnostic labels, such as are at the present time attached to patients on the basis of their presenting symptoms, cannot be taken as any hint of their accessibility or otherwise to psychotherapy. Even with the most severely disturbed patients, much can be achieved by sympathetic and informed interviews, when attention is focused on the original body fantasies and the patient's relation to himself. It is not infrequently possible to reverse delusions, and, if nothing else, psychotherapy may prevent such patients from growing worse.

When patients' anomalous sensations and false beliefs about their bodies are misdiagnosed and treated medically and surgically as if they were due to physical illness, they become permanently fixed by being confirmed and shared by medical opinion. This naturally makes a subsequent psychotherapeutic approach much more difficult.

Effective psychotherapeutic interviews conducted on these lines with most out-patients need rarely to be more frequent than once a week, and in many cases much less often. More severely disturbed patients also may show rapid improvement when their irrational fears and beliefs about their bodies are traced out with them in terms of their relation to themselves. Even delusional systems which seem to refer to the patient's relation to the outside world—usually the only ones elicited at diagnostic interviews—can be found to have originated in fantasies centring on the patient's own body, and are often only the patient's attempts to explain and rationalize what he feels to be going on inside him.

Contact can be made with severely disturbed alienated patients if one can understand them and so enter their world, thus providing a bridge to reality and decreasing their isolation and alienation. The response of such patients, once one has succeeded in making contact with them, unequivocally contradicts the psychoanalytical doctrine that such patients do not form transferences.

Summary.

Hypochondriasis is an extremely common condition, but over the last 50 years psychiatrists have tended to regard it as of little clinical or theoretical importance.

The history of the concept is briefly sketched, and the bases of current attitudes to the subject are examined.

It is suggested that, in fact, hypochondriasis is of considerable importance both clinically and theoretically in psychiatry, and certain views propounded by Macalpine and Hunter in this context are discussed.

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WHY ERGOMETRINE? A REVIEW OF ERGOT IN PRACTICE TODAY.[1]

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Historical Review.

WHO first associated the forcing of pains of women in childbed with the eating of bread made from ergot-infected rye is unknown. In the sixteenth century, German midwives understood that the labour-enhancing properties came not from the true grain, but from the black corns or spurs which grew in the head of the rye. They did not, however, realize that these corns were a parasite and not part of the rye itself. In 1582, Lonicer gave the earliest instructions for the medicinal use of ergot when he wrote:

> . . . . they are held to be a special medicine for women in labour, and for the purpose of awakening the pains, three of the spurs are swallowed.

This precise dose recorded 377 years ago is now of special interest, as three ergot spurs contain, on the average, 0·5 mg. of ergometrine, the dose of the pure alkaloid used in obstetric practice today (Moir, 1955).

[1] Read at a meeting of the Clinical Society of the Royal Hospital for Women, Paddington, on March 10, 1959.

The introduction of ergot to official medicine came from America. Dr. John Stearns, a country practitioner, wrote in the *Medical Repository of New York* of 1808 an account of its use in lingering labour. He ground the ergot spurs to a powder, called it the *Pulvis Parturiens* and gave it to his patients. In using the powder, Stearns advised:

> . . . . previous to its exhibition it is of the utmost consequence to ascertain the presentation . . . as the violent and almost incessant action which it induces in the uterus precludes the possibility of turning[1] . . . you will be surprised with the suddenness of its operation; it is therefore, necessary to be completely ready before you give the Medicine . . . .

So effective was this short-cut for labour that its use soon became widespread. The inherent danger of "the incessant action which it induces" was passed over, and the *pulvis* was given to unsuitable patients, such as those with contracted pelves and malpresentations. Ruptured uterus became commonplace, and an end was not put to this practice until 1813, when Hosack with an apt phrase renamed the *"pulvis ad partum"* the *"pulvis ad mortem"*. The powder was discarded as an adjuvant to labour, though retained for its lesser role in the control of hæmorrhage. It is of interest to note that this powder survives today as the essential ingredient of "Tab. Q.E.S.".

Ergotoxine, Ergotamine, Ergometrine.

No further interest was taken in ergot until morphine was extracted as a pure alkaloid from opium. Then eyes turned once more to ergot, and in 1875 Tanret isolated a pure crystalline substance which he named Ergotinine. Unfortunately ergotinine was physiologically inert. In 1906, Barger and Carr had greater success when they prepared ergotoxine as a pure alkaloid from ergot. Their compound proved active and was used clinically for many years as ergotoxine ethanesulphonate. The next advance came in 1918, when Stoll of Basle isolated ergotamine as an active pure alkaloid from ergot, and this drug took its place along with ergotoxine in the treatment of hæmorrhage.

It was claimed that the active substances in ergot had now been found, and that the pharmacopœial liquid extract should henceforth be standardized for its ergotoxine and ergotamine content. Here, however, was a conundrum, because analysis showed that the official *Extractum Ergotæ Liquidum* B.P., 1918 was prepared in such a way as to leave it entirely free of both these vaunted alkaloids. A correspondence grew up in the medical Press, with the pharmacologists declaring that the liquid extract was worthless (Clark, 1927) and the obstetricians saying how well pleased they were with the current preparation, their trusted friend in hæmorrhage.

With the coming 1932 revision of the British Pharmacopœia this dilemma had to be settled, and the Medical Research Council of the Privy Council approached Professor F. J. Browne, of University College Hospital, for his help in the matter. Laboratory methods had failed in assessing oxytocic activity, and a method with the human subject was needed. The history of the *Pulvis Parturiens* obviously ruled out investigations with these substances in labour, so studies had to be confined to the post-partum period. Professor Browne's then junior, Chassar Moir, observed in the course of routine ninth puerperal day discharge examinations that it was a simple matter to pass a finger through the cervical os. If a finger, why not a small recording balloon? And this he did with gratifying results. He gave ergotoxine and ergotamine to puerperal patients and, with a balloon in the uterus connected through a mercury manometer to write on a revolving drum, recorded the effects of these drugs (Figure I). By intramuscular injection both ergotoxine and ergotamine produced an oxytocic effect after a delay of some 20 minutes. By mouth the drugs were of little value. Moir then tried giving the despised liquid extract by mouth, and a remarkable thing followed (Moir,

[1] *"Turning" means internal version.*

1932 a and b). Four to five minutes after the patient had swallowed the medicine the uterus contracted firmly, and a powerful oxytocic response was recorded which was much more powerful and four times faster than had been the response to intramuscular injections of ergotoxine and ergotamine (Figure II, above). Here, then, in the liquid extract was a hitherto unsuspected substance. Moir recalled the words of Dr. John Stearns: " . . . you will

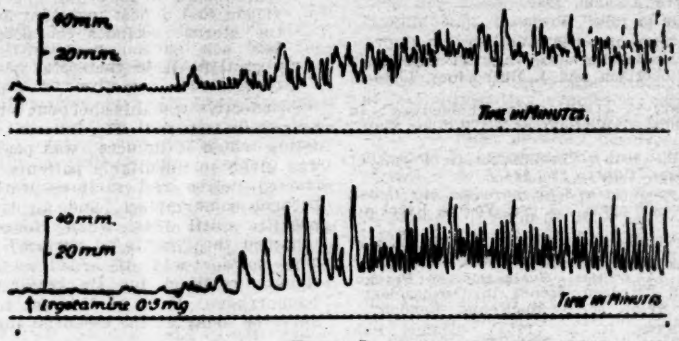

FIGURE I.

Ergotoxine (above) and ergotamine (below) produce a typical slow-acting oxytocic response in the human puerperal uterus. The delay between intramuscular injection and effect on the uterus is just over 20 minutes. (From Moir, 1932a; reproduced by courtesy of the Editor of the *British Medical Journal*.)

be surprised with the suddenness of its operation; it is therefore, necessary to be completely ready before you give the Medicine". The obstetricians were vindicated in their support of the official liquid extract.

Together with an organic chemist, the late H. W. Dudley, of the Medical Research Council, the investigations continued, and after three years of gay hopes but

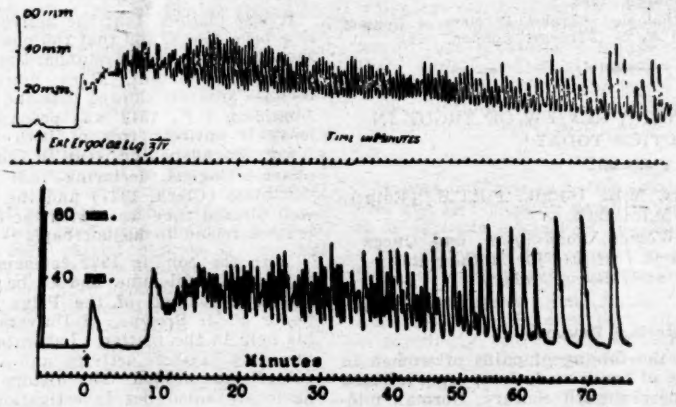

FIGURE II.

The discovery of ergometrine. Oral administration both of liquid extract of ergot and of ergometrine crystals produces a strong oxytocic effect in four to seven minutes. This is in sharp contradistinction to the slow response with ergotoxine and ergotamine. (From Dudley and Moir, 1935; reproduced by courtesy of the Editor of the *British Medical Journal*.)

many false paths, a pure crystalline substance was prepared which had the same dramatic oxytocic effect on the uterus as had the liquid extract (Figure II, below; Dudley and Moir, 1935). On the advice of Sir Henry Dale this substance was called ergometrine. Within six weeks three other groups of workers published their isolation of the same compound. Each gave it different names, but today the original name ergometrine is established.

Now, what has happened in the last 20 years? A whole host of compounds has been prepared (compare Stoll, 1950), but of these, three only have found clinical use. They are methyl ergometrine, dihydroergotamine and "Hydergine".

Methyl Ergometrine.

The yield of ergometrine from crude ergot is low; but by a special chemical process many of the inert ergometrine-like alkaloids present in crude ergot can be converted relatvely easily in good quantities into the active substance, methyl ergometrine. Briefly it may be said that when given by intravenous injection ergometrine acts in 45 to 55 seconds and methyl ergometrine in one and a half minutes. There is little difference when they are given by intramuscular injection, both compounds taking effect after a delay of seven minutes (Gill, 1947; Embrey and Garrett, 1958). Except for intravenous use there is little to choose between the two drugs. It is stated in the American literature that ergometrine raises the blood-pressure and that methyl ergometrine does not do so; but while I have found a number of papers on this subject, none so far has produced figures that will stand statistical scrutiny.

Dihydroergotamine.

As far back as 1906, Dale described the adrenaline-blocking effect of ergot, and this is the second great property

of the ergot alkaloids as a group. All possess it to a greater or lesser degree. Ergometrine, the strongest oxytocic, is almost devoid of adrenaline-blocking properties. Dihydroergotamine is probably the strongest adrenaline-blocking member of the group, and it has been stated that this substance is devoid of oxytocic properties (Rothlin, 1946, 1947; Orth and Ritchie, 1947). Dihydroergotamine has therefore been used in inert labour to block the inhibitory effect of adrenaline said to be present and the stimulatory effect recorded has been attributed to this mechanism (Sauter, 1948; Gill and Farrar, 1951).

There is no doubt that dihydroergotamine blocks the effect of adrenaline on isolated human myometrium, but from that observation it does not follow that a similar effect will be seen *in vivo*. Indeed, the contrary is true; dihydroergotamine has no effect on the uterine response to adrenaline in late pregnancy and labour (Garrett, 1955 *a* and *b*). The statement that dihydroergotamine was devoid of oxytocic activity was based on work with animal uteri; but more careful studies by Moir's method with the puerperal uterus have shown that the action of dihydroergotamine is none other than the well-known oxytocic activity of its parent alkaloid ergotamine, the only difference being that dihydroergotamine is, weight for weight, manifestly weaker as an oxytocic (Embrey and Garrett, 1955).

The following is an approximate quantitative comparison in arbitrary units of the oxytocic activity of the slow-acting ergot alkaloids:

Ergotamine	2·0
Ergotoxine	2·0
Dihydroergotamine	1·0
Dihydroergotoxine	1·0
Dihydroergocristine	0·2
Dihydroergokryptine	0·2
"Hydergine"[1]	0·4

available under the trade-name of "Hydergine" (Sandoz). By its adrenaline-blocking activity "Hydergine" lowers the blood pressure and has therefore been used in the treatment of hypertensive disorders. On slender laboratory evidence it has been held to lack oxytocic activity, and some workers have used "Hydergine" in the treatment of preeclamptic toxæmia (Rupp, 1953; Sauter and Suenderhauf, 1954). However, this is unwise, as simple studies on the post-partum uterus show a definite, though weak, oxytocic action with each constituent of the preparation (see tabulation above).

TABLE I.

The Effect of Giving Ergometrine by Intravenous or Intramuscular Injection with the Crowning of the Head or Delivery of the Anterior Shoulder Compared with Untreated Controls: 7092 Cases from Various Authors.

Author.	Method of Injection.	Ergometrine.		Controls.	
		Post-Partum Hæmorrhage.	Manual Removals.	Post-Partum Hæmorrhage.	Manual Removals.
Lister (1950)	Intravenous.	0·4%	1·6%	4·0%	2·2%
Martin and Dumoulin (1953).	Intravenous.	1·2%	3·0%	13·1%	1·1%
Daley (1951)	Intramuscular.	9·2%	3·5%	15·7%	3·7%
Kimbell (1954)	Intramuscular with hyaluronidase.	0·9%	1·1%	3·5%	1·6%

Present-Day Use of Ergot.

Today in obstetrics the use of ergot is largely the use of ergometrine, as one by one the other members of the ergot group have fallen from favour. We all know of its use after the delivery of the placenta, and most obstetricians use ergometrine at the delivery of the anterior shoulder. I shall not go into the pros and cons of these methods, but shall summarize their results. It would not be an unfair generalization to say that these methods have decimated the post-partum hæmorrhage rate and have doubled the manual removal rate. More accurate figures are given in Table I collected from several authors.

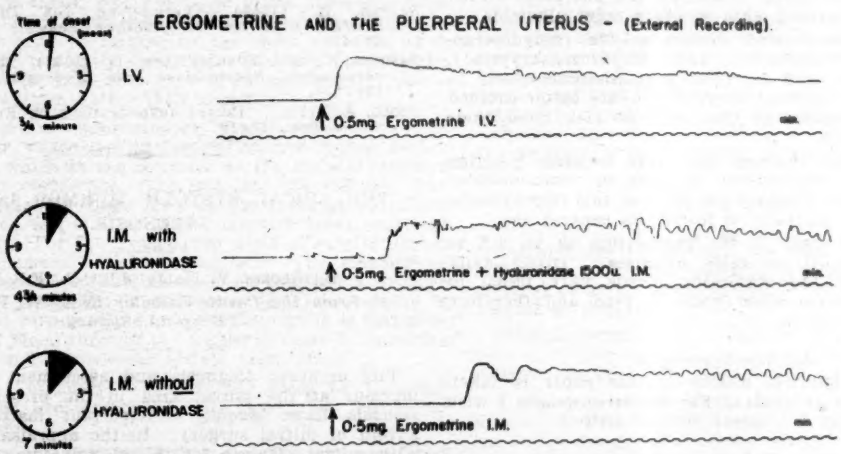

FIGURE III.

The addition of hyaluronidase to the injection of ergometrine shortens the delay between the intramuscular injection and the effect on the uterus. It is questionable whether this procedure is an adequate substitute for the intravenous injection. (From Embrey and Garrett, 1958; reproduced by courtesy of the Editor of the *British Medical Journal*.)

It follows, therefore, that dihydroergotamine has no advantage for use in labour over ergotamine, and from the unhappy history recounted earlier with the *pulvis parturiens*, the unwisdom of such treatment is obvious.

"Hydergine."

A preparation containing equal parts of dihydroergotoxine, dihydroergocristine and dihydroergokryptine is

[1] A mixture of equal parts of dihydroergotoxine, dihydroergocristine and dihydroergokryptine.

Variations on the general theme have been suggested in an attempt to improve these results, but how significant have they been? The addition of hyaluronidase (Kimbell, 1954) certainly reduces the injection-effect delay of the intramuscular injection; but the actual reduction from seven minutes to four and three-quarter minutes (Figure III) is probably outweighed by the extra time taken to prepare the mixed injection (Embrey and Garrett, 1958).

Finally, an everyday question: does ergot hasten involution of the puerperal uterus? The essential feature of involution is atrophy, and if it is atrophy that is required, then rest, not exercise, will be necessary. This is a general rule for the body. Reference to the recordings from puerperal uteri (Figures II and III) shows how ergot "exercises" the uterus by inducing in it a pattern of powerful recurrent contractions. This picture is the exact opposite of what is needed if atrophy and hence involution are to be encouraged. Ergot, therefore, after the risk of hæmorrhage has passed, should be avoided in the puerperium. Even more important is this advice in the case of infected uteri, in which activity induced by ergot may spread the infected material to hitherto uninfected areas. Clinical proof of these contentions has been provided by Moir and Scott Russell (1943), who measured the daily heights of the uterine fundus above the symphysis pubis in the puerperium. They found no advantage in ergot as an aid to involution and recommended that its use be discontinued.

Summary and Conclusion.

1. The development of ergometrine has been reviewed and its present-day use discussed.

2. Methyl ergometrine has a very similar action to ergometrine on the human uterus, but suffers from the disadvantage that there is a slightly longer delay before it takes effect when given by intravenous injection.

3. Dihydroergotamine is an effective sympatholytic drug in the laboratory, but lacks this effect in the intact patient. Its action on the labouring and puerperal uterus is as a simple oxytocic akin to other ergot alkaloids.

4. Other hydrogenated ergot alkaloids (dihydroergotoxine, dihydroergocristine and dihydroergokryptine), which have been used for their sympatholytic effects in the treatment of essential hypertension, are better avoided in pregnancy because of the inherent risk from their oxytocic properties.

5. Hyaluronidase shortens the delay between injection and effect when ergometrine is given by intramuscular injection; but it is questionable whether this improvement is of sufficient magnitude to justify its general use.

6. The use of ergot in the puerperium as an aid to involution is based on false premises. Direct daily measurements of the involuting uterus have failed to show any advantage when ergot is used and therefore support this contention.

Acknowledgements.

The earlier historical matter in this paper is taken largely from Barger (1931). For the later details I wish to thank Professor J. Chassar Moir of Oxford.

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THE APICAL SYSTOLIC MURMUR IN MITRAL STENOSIS.

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The accurate diagnosis and assessment of a systolic murmur at the mitral area in the presence of mitral stenosis have become all-important matters with the advent of mitral surgery. In the appraisal of a patient with mitral stenosis for mitral valvotomy, the presence of a mitral systolic murmur looms large, especially when the systolic murmur is of impressive intensity. The commonest cause of such a murmur is associated mitral incompetence.

Mitral Incompetence.

The criteria for the diagnosis of an important degree of mitral incompetence have been clearly set out by many authors, for example, Brigden and Leatham (1953) and Logan and Turner (1952). These include the hyperdynamic or heaving cardiac impulse at the apex, which may be displaced to the left, the loud apical pansystolic murmur embracing both first and second heart sounds, which may be accompanied by a palpable thrill, and finally, in some cases, a loud third heart sound. All these criteria are not always present, and, in fact, on occasions only the

murmur may be present. It is of prime importance, therefore, to note all the details of this murmur.

This pansystolic murmur is usually loud and of fairly high frequency. It is maximal at the apex beat over the surface of the left ventricle and is conducted towards the axilla; sometimes it is transmitted posteriorly. The murmur begins with the mitral element of the first heart sound, for the regurgitation begins as the mitral valve tries to close. The murmur of mitral incompetence must continue well into the time of closure of the aortic valve, for there is still a strong pressure gradient across the mitral valve at that time. It therefore embraces the second as well as the first heart sound.

It is most important that the murmur should be auscultated during inspiration and expiration. The murmur is loudest on expiration and diminishes on inspiration, the point which distinguishes it from the murmur of tricuspid incompetence, in which the reverse is the case. The murmur of mitral incompetence is diminished during inspiration, because during this phase of respiration the pulmonary blood pressure falls, owing to increased capacity of the pulmonary blood vessels. In consequence there is a temporary reduction of the blood flow into the left auricle, and less blood flows through the mitral valve. The converse is the case during expiration. In my experience the murmur most likely to be confused with the murmur of mitral incompetence is the murmur of tricuspid incompetence.

Tricuspid Incompetence.

The criteria for the diagnosis of tricuspid incompetence have also been clearly set out by a number of authors (Muller and Shillingford, 1954). The physical signs include a characteristic jugular pulse with a large *V* wave followed by a rapid *Y* descent, and a conspicuous *Y* trough. There may be systolic pulsation of the liver synchronous with the large *V* wave, a lift or heave palpable over the right ventricle, and a pansystolic murmur with or without a thrill, which may be heard anywhere from the tricuspid area and the left sternal edge to the apex beat, which may be formed by the right ventricle when this chamber is greatly distended. The apex beat may be displaced to the left—it is tapping or occasionally "turbulent" in character, rather than heaving.

The important differentiating point, however, is that the murmur waxes during inspiration and wanes during expiration, which is the converse of the systolic murmur of mitral incompetence. The fact that the murmur may be heard over the same area as the murmur of mitral incompetence, and is of the same character, may well lead to confusion. For this reason, the effect of respiration on the two murmurs is most important. The murmur of tricuspid incompetence is increased on inspiration, because during this period the intrathoracic negative pressure is greatest and venous filling of the right auricle is maximal. The flow of blood through the tricuspid valve is therefore greater when the auricular systole takes place.

The great majority of recognized cases of tricuspid incompetence are associated with auricular fibrillation (Wood, 1956).

In the first 300 patients with mitral stenosis considered at our clinic, there were 11 who were initially rejected or deferred for operation on account of a mitral systolic murmur, which ultimately turned out to be the murmur of tricuspid incompetence. The important point is that in nine of these cases the tricuspid incompetence was proved at operation or autopsy to have been functional, and to have been secondary to a severe degree of mitral stenosis. Eight of these patients were submitted successfully to valvotomy, and the patients have done spectacularly well. The ninth patient came to autopsy before operation could be carried out. The patient was a boy, aged 18 years, who was found to have had congenital mitral stenosis with functional tricuspid incompetence.

In congenital mitral stenosis, the classical apical diastolic murmur of mitral stenosis is rare (Ferencz, Johnson and Wiglesworth, 1954). The most interesting sign is that of a systolic murmur at the apex (Bernstein, Weiss and Lawrence, 1958).

With the hypoplastic left ventricle which is usually present in congenital mitral stenosis, and the almost invariable association of pulmonary hypertension, the apex is represented by the right ventricle. In this case, as in the majority of cases, the apical systolic murmur probably arises from the tricuspid valve.

All patients undergoing operation had a high pulmonary vascular resistance. This is a most important differentiating point in doubtful cases. Mitral incompetence is improbable in patients with extreme pulmonary vascular resistance (Wood, 1956). Functional tricuspid incompetence is rare in the absence of extreme pulmonary resistance. It is worthy of note that organic tricuspid incompetence without some evidence of tricuspid valve stenosis is rare (Wood, 1956).

The two commonest causes of functional tricuspid incompetence are pulmonary hypertensive mitral stenosis and atrial septal defect, but it may occur when there is right ventricular failure from any cause. When tricuspid incompetence exists in the presence of mitral stenosis, it usually means that the patient has severe hypertensive mitral stenosis which urgently needs valvotomy.

Apart from the pansystolic murmur, which waxes during inspiration, and the presence of high pulmonary vascular resistance, there are other points, clinical, radiological and electrocardiographic, which may favour the diagnosis of tricuspid incompetence rather than of mitral incompetence. These include the absence of a left ventricular type of apex beat and the presence of signs of pulmonary hypertension, such as a conspicuous *A* wave in the venous pulse, a lift over the right ventricle and an accentuated pulmonary second sound, and the presence of a mitral opening snap. A right-sided electrocardiogram and radiological signs such as an enlarged right ventricle and Kerley's lines favour the diagnosis of functional tricuspid incompetence rather than that of mitral incompetence.

The difficulties of diagnosis may be increased by the fact that signs of mitral stenosis may be made inconspicuous by pulmonary hypertension and auricular fibrillation associated with a severe mitral valve lesion. It is most important, therefore, in cases of tricuspid incompetence to listen with great care for the signs of mitral stenosis. This implies the use of exercise and posturing in conjunction with careful auscultation at the mitral area.

Aortic Stenosis.

Other apical systolic murmurs which may occur in mitral stenosis include the aortic systolic murmur. Clinical differentiation of this murmur may be difficult when the murmur of aortic origin is audible only at the apex, or is loudest at this site.

Clinical features of the murmur of aortic stenosis which help to differentiate it from the murmur of mitral incompetence can be briefly summarized as follows:

1. The murmur of aortic stenosis is shorter and mid-systolic in time, starting when the aortic valve opens at the end of the period of isometric contraction and finishing appreciably before the aortic sound, whereas the murmur of mitral incompetence is pansystolic and embraces the second sound.

2. The aortic systolic murmur is often high-pitched and "seagull" in character, although, less frequently, the murmur of mitral incompetence may be "seagull" in type.

3. Some other signs of aortic stenosis are likely to accompany the aortic systolic murmur, and these include the characteristic plateau pulse and the low pulse pressure. A systolic ejection click immediately precedes the murmur in some cases, these usually being cases of relatively mild degree (Wood, 1958).

When the diagnosis is doubtful the amyl nitrite test suggested by Barlow and Shillingford (1958) may be useful. I have confirmed this in three cases. During the first 15 to 20 seconds after the inhalation of amyl nitrite,

the murmur of mitral regurgitation diminishes in intensity and duration. These changes last for at least twenty seconds, and then the murmur returns to its original state. However, the systolic murmur of aortic origin remains unchanged or increases slightly during the first twenty seconds after the inhalation. The mechanism of the reduction in the intensity of the systolic murmur in mitral regurgitation may be lowering of the peripheral resistance, which allows a relatively greater part of the stroke volume to pass forward through the aortic valve. Similarly, the increase in the aortic systolic murmur may be due to an increased stroke output. Kahler (1932) holds that there is a decrease or disappearance of the systolic murmur of mitral incompetence after the inhalation of amyl nitrite; this differentiates this murmur from the majority of functional systolic murmurs, which increase with amyl nitrite. If it is suspected that the murmur is arising from both aortic and mitral valves, a more accurate interpretation of the effect of amyl nitrite may be obtained with two observers, one listening at or inside the apex and the other outside the apex towards the axilla. The second observer will hear the regurgitant murmur fade within the first 20 seconds, whilst the first will hear the ejection murmur of aortic stenosis increased approximately between 25 and 40 seconds.

Phonocardiography, when available, confirms clinical findings and demonstrates the diamond-shaped murmur of aortic stenosis ending before the second sound, as compared with the pansystolic murmur of mitral regurgitation, which frequently includes the second heart sound.

Surgery and Mitral Regurgitation.

Finally, patients should not be rejected for mitral valvotomy purely on the grounds of a mitral systolic murmur, even if it is believed that this murmur is due to mitral regurgitation. Frequently a rigid and obstructed mitral valve with a button-hole orifice will give rise to a systolic murmur without there being any gross degree of mitral regurgitation. The degree of mitral regurgitation existing may be eliminated or lessened when this type of valve is split. In other cases, although the regurgitation will not be diminished, it will not be increased, and the ill effects of the mitral valve obstruction will have been overcome. When there are no signs of gross mitral incompetence apart from a mitral systolic murmur, and when the signs of mitral stenosis are compelling—particularly when they are associated with signs of pulmonary hypertension—exploration of the valve is often justifiable.

However, this is often one of the most difficult decisions to make in cardiology. One of the commonest causes of poor results from the operation of mitral valvotomy has been shown to be pre-operative selection of patients with an excessive degree of mitral incompetence (Wood, 1954; Ellis *et alii*, 1957).

Numerous technical procedures have been suggested to assist in assessing the degree of mitral incompetence as compared with the degree of mitral stenosis. Direct measurement of the gradient across the valve presents a technical problem. Indirect measures, such as dye dilution curves, have as yet not proved to be completely reliable.

However, Marshall, Woodward and Wood (1958) pointed out that a large *V* wave in the pulmonary artery wedge pressure pulse tracing taken at cardiac catheterization seems to be strong evidence, when diagnosis is doubtful, that the mitral incompetence is the predominant lesion. This has been confirmed by us at operation in several recent cases. With the fuller development of open heart surgery, exploration of the doubtful mitral valve might be more readily undertaken. Plastic repair of severely incompetent valves is now a practical proposition.

Summary.

1. The most difficult problem in the assessment for surgery of patients with mitral stenosis is the decision regarding the significance of a systolic murmur audible at the mitral area.

2. Mitral systolic murmurs do not by any means always represent mitral incompetence. The murmur of functional tricuspid incompetence is frequently confused with the murmur of mitral incompetence. The murmur of aortic stenosis may often be prominent at the apex.

3. A careful study of the clinical characteristics and associations of the murmurs of tricuspid incompetence and aortic stenosis will differentiate them from the murmur of mitral incompetence.

4. Even when an apical systolic murmur is believed to be due to mitral incompetence, patients with mitral stenosis should not be automatically rejected without full consideration. In some cases in which mitral stenosis is the predominant lesion, mitral valvotomy may be of great benefit in overcoming the stenosis, and it may not increase the incompetence. In cases in which there is doubt as to the relative degree of mitral stenosis and incompetence, surgical exploration of the valve is justifiable. This decision, however, should not be made lightly. Certain technical procedures may be of assistance in making this difficult decision.

Acknowledgement.

My thanks are due to Mr. H. M. Windsor for details of findings at operation.

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THE CHALLENGE OF THE CHILD: THEN, NOW AND WHEN?[1]

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WHEN we wonder if we are advancing in any endeavour, it is heartening to pause, look back and consider how far we have come. We well remember among the grim Owen Stanley Ranges in the middle of New Guinea how often the ridges over the Kokoda Trail seemed unattainable. We would halt our plodding feet, turn and look down to the deep valleys in the jungle we had left below, and our burdens became lighter and with good heart upwards and onwards we climbed. So tonight we shall see how far we have come in our consideration of child welfare and where we are now, and perhaps gain a glimpse of what lies ahead. Only when a commodity becomes rare do we generally consider it worthy of regard. I am informed that lying around in the diamond fields of Africa are so many rough gems that, were they gathered and made available, diamonds would be dross. So it was with child

[1] An address delivered at the opening of the Jubilee Mothers' and Babies' Health Association of South Australia, Adelaide, September, 1959.

life until about one hundred and fifty years ago. The world's population appears to have remained fairly constant until the dawn of public health as a national responsibility, and the first public health Act in England was passed in 1848, only 111 years ago.

With the little regard for family restriction that existed, together with the little knowledge of the nature of disease and the complete ignorance of the science of nutrition, babies came into the world in their millions, and as they came so most of them went — many accompanied by their mothers. There were no reliable records before the middle of last century; but it is probably an understatement to say that not half the babies born even at that time lived to see their first birthday. Even did they survive their hazardous appearance, until one hundered years ago none could expect to live beyond the age of forty.

There were many factors contributing to this dismal picture, but the two main forces were disease and malnutrition. A young baby has been described rather cynically as something wrapped around a bowel. Certainly a baby's contentment or misery depends largely upon the condition of his stomach and bowel content. Bowel infections are broadly the result of dirty food, and while most food elements, including milk, are generally clean in their natural state, by careless handling and preparation they are readily contaminated. The history of infant feeding is a fascinating study. Among primitive tribes breast feeding by the mother has been, and still is, the usual practice, complemented early with vegetables and cereals. The duration of lactation varies from a few months among the Hottentots up to fifteen years among the Greenlanders, where a mother may be breast feeding three or four children of different ages. Many of the early civilizations—Egypt, India, Israel, Greece and Rome—have left records indicating the importance they attached to breast feeding and the rules to be observed; but wet nursing and use of milk of animals, such as cows, goats, asses, mares and camels, were ancient practice. With the Renaissance, which began towards the close of the fifteenth century, much of this early teaching, which had survived in the Arab areas, flowed into the Western world. One of the earliest medical books to be printed in the English language was Thomas Phair's "The Boke of Chyldren"—the first pædiatric treatise written by an Englishman. Phair was a lawyer as well as a doctor of medicine of Oxford. This book, with its quaint terminology and herbal therapy, and with the strange wisdom of a man who died in 1560, remains today something more than a medical curiosity. He advocated breast feeding in these words:

> Wherfore as it is agreing to nature so it is also necessary and comly for the mother to nourse the owne child. Whiche if it may be done, it shall be moste commendable and holsome, if not ye must be well advised on taking a nourse not of ill complexion and of worse manners, but such as shalbe sobre, honeste and chaste, well fourmed, amyable and chearefull, so that she may accustome the infant into mirth, no drunkarde viceous nor shiftys she for suche corrupteth the nature of the chylde.

Over the following years many pædiatric publications appeared; but in spite of this spate of advice, when the majority of parents could not read and heeded little beyond traditional superstitions and witchcraft, most babies had to face the hazards of wines, spirits, strong beer, roast pork, opiates, pap and panada—cereals cooked in broth, sweetened with honey and often chewed by the parent or nurse before being ladled into the infant. When we realize the appalling absence of sanitation as we know it, the dreadful mortality among infants at that time is understandable.

There had been faint rumblings over the years against the acceptance of this deplorable state of affairs, but practically no progress was made until the middle of the eighteenth century, abount two hundred years ago. Attempts had been made to improve midwifery, but the care of the baby and child was almost non-existent. Wet nursing was a thriving trade, and many women cast aside their own babies to earn a few shillings each week. In the streets and down the by-ways these abandoned infants were found in their thousands. During one day in London, two hundred years ago, 161 infants were picked up. Until Captain Thomas Coram established the Foundling Hospital in 1741, the fate of these foundlings was deplorable. Those of you who know London House in Guilford Street have probably realized that this institution stands upon ground hallowed by the memory of this great humanitarian. During the seventeenth and eighteenth centuries, it was not fashionable for ladies who considered themselves of quality to breast feed their babies—the eternal social round was not compatible with such a practice. Only with the execution of Margaret Waters in 1870—a notorious baby farmer who was found guilty of killing many babies—did the evil practice of neglecting maternal responsibilities decline.

William Cardogan, George and John Armstrong and Lettsom raised their voices in this crusade for child care. In 1769, the first dispensary for infant poor was opened in London, the forerunner of what we now know as the child welfare centre. The community's conscience was slowly stirring; then came the blackness of the industrial revolution and the seeds withered.

Until the dawn of the last century, England had developed and prospered as an agricultural country—very little food was imported. With the realization of the power of steam by James Watt, and with the invention of the steam engine, the industrial age was born. With the weaving inventions of Arkwright, Hargreaves, Crompton and Cartwright, it developed. With Smeaton and Cost's advances in iron manufacture it prospered. The whole economy of the country was changed. The crafts of the humble homes were consumed in the relentless maw of the machine. Factories arose, and around these factories rapidly grew urban communities under conditions of gross squalor and degradation, at a time when the welfare of the individual devolved upon the impoverished local parish. Little children were put out to work. Boys and girls of five and six years of age were employed in the mines, sometimes harnessed to trucks of coal down in the depths. Not until 1819 was it illegal to employ a child under nine. In 1825 it was legal to work children ten years old for twelve hours a day excluding meal times, but only for nine hours on Saturday. That was less than a hundred and fifty years ago. The prosperity of England appeared to depend upon keeping children at work under deplorable conditions for seventy hours each week.

The outlook for an infant was critical; but in times of crises the United Kingdom has the happy ability to produce the right people. The passage of the Reform Bill in 1832 made possible legislation concerning human welfare. Behind this early legislation was Edwin Chadwick, a young lawyer. Chadwick, and Thomas Southwood Smith, a Scottish doctor, were the founders of the public health system of Great Britain. After the passing of the *Births and Deaths Registration Act* of 1836, Dr. William Farr founded the study of vital statistics, and for the first time something approaching reliable figures was available; these presented indubitable and distressing facts concerning the state of the nation's health. Public clamour demanded action. Charles Dickens entered the lists with "Oliver Twist", and later Charles Kingsley with "The Water Babies". Gradually Parliament decreed that health was a national problem, and here Lord Ashley, Earl of Shaftesbury, was the champion of the child.

But we must remember that Pasteur's epoch-making studies relating communicable diseases to living organisms were not presented to the world until the latter half of last century—less than a hundred years ago. Lord Lister's application of these studies followed even later. The scientific study of nutrition was equally hidden behind the veil. The consequences of vitamin deficiencies were understood only in the early years of the present century. Without the basic understanding of the nature of infectious diseases and of nutrition, legislation alone could not possibly succeed, and the infant mortality during the second half of the nineteenth century actually increased. Hard on the heels of Parliament came the medical profession. Pædiatric teaching as such appears to have begun

at Manchester as early as 1829. In 1852, the Children's Hospital, Great Ormond Street, London, was founded, and in 1857 children's wards in general hospitals were opened in Liverpool; but the first chair of diseases of children in the British Empire was founded only in 1906, at King's College Hospital. In 1876 your own Adelaide Children's Hospital began its splendid record of service.

As a result of the success of the French enterprise directed to the care of artificial food for infants, depots were established at the turn of the century throughout the United Kingdom. These were conducted by municipalities and by voluntary bodies to provide a satisfactory milk supply. These depots developed into centres for advice to mothers concerning feeding and hygiene problems, and by 1906 these became known as infant welfare centres. Three years later your association was founded, and the name of Dr. Helen Mayo must always be remembered in connexion with this movement, as in Victoria the memory of Dr. Isabella Younger and in New Zealand that of Dr. Truby King. War was declared on ignorance, disease and malnutrition affecting infants. At the turn of the century, of every thousand babies born in Australia, about one hundred died in infancy. Now, during the last few years, the figure of infant mortality has remained at about 20 per thousand live births. During last year, 1958, approximately 230,000 babies were born in Australia, and this reduction in infant mortality represents a saving of more than 18,000 lives during that year.

It is worth while to review the vicissitudes of this campaign. At first, faced with ignorance and lack of care, when old traditions were dying hard in the overwhelming advance of science, we rather turned to the laboratory and mathematical exactitude for the sole solution of our problems. As a result, the baby as a human being was often forgotten, and at times the mother was left out of the picture altogether. From the very beginning, I understand you entitled your activity "The Mothers' and Babies' Health Association"—not so with similar activities in certain other States, which were known as "The Baby Health Service." Just as in the past nurses had made a fetish of red flannel, binders and swaddling clothes, we bowed down and worshipped weights and measures, calories and graphs, forgetting that no two babies were ever exactly alike. Some are active, hungry and healthy; others, more sedate, are less hungry, but just as healthy. Some are satisfied and content with long intervals between feeds; others are not. John Armstrong two hundred years ago advised us to follow nature instead of driving it.

When my own first child came along, she behaved according to the rigid rules I had been teaching my students, and my wife and I thought I was rather good. When number two came along, an equally healthy and progressive baby, most of these rules just had to go overboard, and my wife and I began to doubt my infallibility. The more one studied babies themselves and used one's common sense, the less one relied upon mechanical or mathematical devices to record their progress. The more babies one really studied, the more one realized that normal health was a broad area, and not a narrow line, to be trodden with trepidation, from which the least deviation to either side plunged us into disaster. Normal health is a broad road and should be measured by function, not by form. What a child does means far more than what he measures. There is nothing masonic about health; as Lord Horder wrote: "The man who talks about the secret of health is either a crank or is trying to sell you something." In certain dining places when one looked at the bill of fare, one found the caloric value of each serving printed for one's edification. However helpful this may have been for those in certain forms of ill health, can you conceive anything better designed to dull one's appetite and at the same time precipitate indigestion?

A baby, whether he was active or calm, was permitted a certain scale of calories, and whatever the temperature, hot or cold, a certain number of fluid ounces. If the baby was breast fed, he was snatched from the breast at intervals and weighed upon more or less accurate scales—the sole arbiter of sufficiency, whatever the satisfaction of the baby or the comfort of the mother. If breast milk was not available—and I am sure it was frequently inhibited by this procedure—there were elaborate and, to many mothers, quite unintelligible tables involving decimals and fractions. We claimed to "humanize" cow's milk, forgetting that a calf doubles its weight within weeks, the baby within months, and each maternal nourishment is designed accordingly. Cow's milk is cow's milk and breast milk is breast milk and there is nothing we can do to make one either chemically or physiologically exactly similar to the other; nor need we try. All those hours of anxiety and industry measuring drops of this and fractional or decimal additions of that were wasted hours. Of course, many of these fantasically fed babies progressed well; but many mothers suffered, as did their domestic duties and their husbands. I believe I should have lost a deal of my practice had my mothers stopped weighing their well babies. Many a doctor has been rung by a sobbing mother, generally at night, with the complaint: "Baby has gained only one ounce this week". Queries as to sleep, contentment, vomiting, bowels, etc., generally brought perfectly satisfactory answers; but the distressing fact remained that the weight did not coincide with the laid-down line. We have all known infants when they commence to be very active who do not adjust their metabolism for a while and gain little for a few weeks, and yet are perfectly healthy.

Laboratories, weights and measures we now realize should not be masters, but servants, and however accurate their findings, these still require a human intelligence to apply them to a human being. Not only did all this bother exasperate and exhaust the mother, but I wonder how much of this fuss about normal function affected the child. How many of the so-called feeding problems of late infancy and childhood—those difficult little children who would not eat unless the radio blared forth or the whole family danced and sang "ring a rosy" around the table—were the products of this much ado about nothing? I wonder if any of you have visited the Bolton Borough School in Lancashire for delicate children? There are about a hundred and twenty boys and girls from the age of seven years, neither retarded nor physically handicapped. The majority suffer from asthma; recently one little lad had a gastric ulcer. Many had spent a deal of their short lives in hospital or on strict diets and rigid régimes. It may be over-simplifying their problems to state that their main disabilities were over-mothering and over-fathering; but when they are treated as practically normal children, under the weekly supervision of a very sensible doctor—not a psychiatrist—the results have been remarkably satisfactory.

Also, upon the band-wagon of pseudo-scientific worship leapt business enterprise. One had only to open a magazine or regard the hoardings to be disturbed and alarmed at the dangers about to descend upon us, did we rely upon commonsense and simple ordinary foods. Time-consuming and expensive substitutes were offered, requiring little if any digestion by the baby, and certainly providing no encouragement for teeth. It is a tribute to our toughness that so many babies survived this onslaught. Personally, I believe it is the encouragement of breast feeding and the great improvement in the cleanliness of artificial foods, rather than in their composition, that has brought about the wonderful advance in infant welfare, and now the mother is brought more and more into the picture. However, there still lingers in certain maternity hospitals and wards the strange practice of separating the mother from the new-born baby. Having survived the hazard of the actual birth, the baby is hurried away and secluded in a common nursery. The mother—especially if experiencing her first confinement—having succeeded after nine months' devotion and anxiety in the most wonderful achievement in the world, a baby, is left alone to wonder, as she always does: "Is he all right? I see him only for a few minutes at feeding time." If the father and the relatives wish to see the child—as surely they are entitled to do—the labelled baby is held up for a brief

space behind a large glass window. How undignified! How like the snake cage in the zoo! This practice arose because of the mistaken fear of disturbing the mother and the dread of infection. Compare the contentment of a young mother who has her baby beside her with the anxiety of the lonely mother, deprived, except at prescribed feeding intervals, of the chance of developing and bestowing her wonderful maternity upon her baby, and you will have no fear as to any disturbance. As to infections—how many babies beside their mother day and night become infected, compared with those confined and often crammed in a common nursery, where at times dangerous and fatal waves of infection have swept through the crowded bassinets? A recently published study by Jennifer K. Burden, from the Department of Obstetrics in your own University, has given a careful and convincing answer to what I hope will be a rapidly disappearing practice.

And so, over the difficulties and frustrations of the last fifty years, your service and that of similar associations in Australia and elsewhere are emerging triumphant. Enriched with a wealth of scientific advancements, humanity and common sense are on the road to victory. But we should not remain complacent. Infantile mortality, as I said, has remained fairly stationary over the last ten years—round about 20 per 1000 of live births; but the picture is changing. Such are our rising standards of living, our prosperity, our widening knowledge of nutrition and our education facilities, that mass malnutrition should no longer be with us as a stigma. With health services second to none in the world, in a country where sunshine and clean air are so bountiful, when immunization facilities against many of the devastating diseases of the past have dispersed their terrors, the problems we faced fifty years ago are no longer with us to any great degree. The introduction of the life-saving antibiotics—again a field pioneered by your own Sir Howard Florey—has been an incalculable boon. However, there is a growing and widespread uneasiness concerning the dangers of the indiscriminate administration of these substances as an easy way out in relatively harmless conditions which would almost certainly respond to simpler care. More than 1000 deaths from penicillin have been reported in the United States, and it is estimated that about 5% of patients have disturbing side effects. Vast and very expensive children's hospitals are being built throughout Australia; but when you are raising your millions for these modern structures, may I remind you that most hospital buildings have proved to be outmoded in many respects within twenty-five years? The worth of any hospital is determined solely by the care and kindness the patients receive, by the teaching that is conducted and by the advances achieved in medical science. A few years ago, in Newcastle-on-Tyne, the late Professor Sir James Spence wanted a baby hospital for the Durham Medical School, but little money was available. For a relatively small sum, he acquired a terrace of houses in an area of ill repute. With the minimum of reconstruction, but with adequate paint and plumbing, he established his hospital. It was far from ideal in many respects, but if any of you were privileged to visit that hospital, you always found happy and contented mothers living in with babies who were generally well on the way to health.

Chairs of child health are being established in our universities and filled by splendid men—our own graduates—into whose hands we can confidently entrust the training of those coming after us. We are honoured tonight by the presence of the latest appointee to this responsible position—Professor Vernon Collins, of the University of Melbourne. Pædiatricians are now included among the staff of our women's hospitals, to direct the care of the new-born. The most recent appointment in Melbourne at the Royal Women's Hospital has gone to a man who has no senior degree, but who is most highly qualified by his vast knowledge and experience, his personality and his humanity. In other words, a true sense of value has influenced this appointment, rather than a deference to that sometimes dangerous disease, multiple generalized diplomatosis.

Vast sums are now available for research. It is right and proper that money should be found for costly equipment and accommodation necessary for certain avenues of investigation not possible without these facilities. But may I remind you that money cannot buy brains? The beginning of many great medical advances has resulted from the consideration of long-existing facts, waiting for their perception and coordination. This was most delightfully shown by Dr. Clive Fitts in 1958 in his Sir Richard Stawell oration. The appreciation of the power of antibiotics was one of the outstanding examples of serendipity, which came only to the trained mind of Sir Alexander Fleming. Let me instance also the momentous contribution by another Australian, Sir Norman Gregg. With no special or costly equipment or facilities other than his searching, rare intelligence, with the expenditure only of time and contemplation on facts which had been before all of us, but which we had failed to regard, he pronounced on the effects upon the unborn child of rubella during the early months of pregnancy. The whole world awoke to what it had been blind to. Who can compute the malformations and misery that have been saved by his achievement?

Surely, then, with these advances we can face the future with confidence; but let us not remain satisfied, content to coast along with our present steady low infant mortality. As His Excellency Field-Marshal Sir William Slim has reminded us, there is only one direction in which anyone can coast—downhill. The challenge remains. What will be the effect of our migration policy, which has resulted in the influx of more than a million newcomers to our country during the last twelve years? One in every 10 people in Australia has come recently from Europe, and of one in every five babies born here now, one or both parents are migrants. Most have never previously enjoyed conditions approaching our own. Many, during world wars and since, have suffered hardships and privations such as we have never known. What effect will this impact have upon our over-all child health? It is far too early to pronounce, but a demological survey has so far failed to reveal any setback in our remarkably changed community.

Fifty years ago, with few exceptions, mothers were in their homes with their children. When a girl married, she automatically retired from her employment, developed her home and cared personally for her family. Nowadays, almost from the altar we may find girls back at their jobs, living with mother or in a tiny flat. The reason or excuse usually given is "we are trying to buy or build a house" or "we have so much on hire purchase and time payment, I must work", and many defer the advent of a family until the house has been achieved, or the car and the television set have been paid for. Unfortunately, some find that after such a postponement the family just does not happen. Surrounded with all those things they would not do without, the parents live their unsatisfied lives. If the family comes along before the home, Granny, some other kindly relative, or the woman next door does the caring in the daytime, and mother and father return to find the children almost asleep, having left in the morning before they are properly awake. A deal of attention is being directed at present to the effect of broken homes; in the domestic establishments to which I have referred a home is not even built. In my opinion, this has an enduring effect upon the infant and upon the child. I do not know quite what we can do about it, except to do all in our power to facilitate the provision of homes for newly-weds and to encourage them to accept parental responsibilities.

An infant and a child should always be considered as a member of a family unit, living within and being profoundly influenced by the environment of the family home. When I was teaching students in a children's ward, I always advised them to visit the home of any patient, to appreciate the environment and personalities from which the child had come and to which he would return on recovery. Only then did I consider that we were fitted to discuss the child's condition and endeavour to help in restoring normal health. I look forward to the time when

father, and perhaps Granny, and even the woman next door, will be included in any activity directed to child welfare.

The majority of infantile deaths now occur during the first month of life from congenital malformations, birth injuries, neonatal infection and immaturity. After this age accidents rear their ugly heads and are responsible for the majority of deaths under the age of fourteen years—a horrible and disgraceful fact. Wounds, burns, scalds, poisonings, drownings and electric shocks are the main culprits. A survey by the Royal Children's Hospital, Melbourne, a few years ago, among 20,000 homes, revealed at least one significant accident to a child among 12,000 of them. One in 10 of all admissions in this hospital is the result of accidents. In my own State of Victoria, within the greater metropolitan area last year, the highest incidence of infant mortality was not within the less privileged industrial areas, but in St. Kilda, a residential seaside area of good homes and heavy traffic.

The result of any accident, not only life or death, but also the extent and duration of any disability, depends very largely upon what is done at once. Unfortunately in Australia not one in every hundred of us is qualified to apply adequate first aid to the common everyday accidents. Every responsible citizen, man and woman, lad and lass, should be so trained. Only when everyone realizes the daily hazards in our homes, on the roads and in the waters, and contributes to avoiding them and knows what to do at once if they occur, will the present disgraceful tally of avoidable slaughter and suffering be reduced.

These, then, are some of the problems that lie ahead, but there is a stirring conscience deep in the community. After an orgy of wars, nations have united for the first time in the world's history in a universal declaration of human rights. Earlier in 1959, in April, the United Nations, recognizing that "whereas the child needs special safeguards, including special legal protection, by reason of his physical and mental immaturity, and whereas mankind owes to the child the best it has to give", has pronounced "The Charter of the Child", as follows:

> The General Assembly recognizes and proclaims the essential rights of the child to the end that he may have a happy childhood and be enabled to grow up to enjoy for his own good and for the good of society the fundamental rights and freedoms, particularly those specified in the Universal Declaration of Human Rights, and calls upon men and women as individuals as well as upon local authorities and national governments to recognize and strive for the observance of those rights through the application of the following principles.
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> 1. The child shall enjoy all the rights set forth in this declaration without distinction or discrimination on account of race, colour, sex, language, religion, political or other opinion, national or social origin, property, birth or other status, whether of himself or of either of his parents. All children, whether born in or out of wedlock, shall enjoy these rights.
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> 2. The child shall be given the means necessary to enable him to develop physically, mentally, morally, spiritually and socially in a heathy and normal manner and in conditions of freedom and dignity.
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> 3. The child shall enjoy special protection by law and by other means. Whenever necessary, opportunities and facilities shall be provided by law to enable him to develop in accordance with the principles of this Declaration. The best interests of the child shall be the paramount consideration in the enactment of such laws.
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> 4. The child shall be entitled from his birth to a name and a nationality.
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> 5. The child shall enjoy the benefits of social security. He shall be entitled to grow and develop in health; to this end special care and protection shall be provided both to him and to his mother, including adequate prenatal and post-natal care. The child shall have the right to adequate nutrition, housing, recreation and medical services.
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> 6. For the full and harmonious development of personality, the child needs love and understanding. He shall, save where his best interests require otherwise, grow up in the care of his parents, and a young child shall not, save in exceptional circumstances, be separated from his mother. In any case, opportunity shall be provided to the child to grow up in an atmosphere of affection and moral and material security. Society as well as public authorities shall have the duty to extend particular care to children without a family or those without adequate means of support.
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> 7. The child is entitled to receive free and compulsory education, at least in the elementary stages. The education of the child shall be directed to the full development of his personality and the strengthening of respect for human rights and fundamental freedoms; it shall enable him, enjoying the same opportunities as others, to develop his abilities and individual judgement and to become a useful member of society. It shall promote mutual understanding, tolerance and friendship among all peoples and racial or religious groups, as well as understanding of the culture both of his own people and of other peoples and of the principles and purposes of the United Nations. The best interests of the child shall be the guiding principle of those responsible for his education and training; that responsibility lies in the first place with his parents.
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> 8. The child shall in all circumstances be the first to receive protection and relief.
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> 9. The child who is physically, mentally or socially handicapped shall be given the special treatment, education and care required by his particular condition.
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> 10. The child shall be protected against all forms of neglect, cruelty and exploitation. He shall not be admitted to employment before an appropriate age; he shall in no case be caused or permitted to engage in any occupation or employment which would prejudice his health or education or interfere with his physical, mental or moral development.
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> 11. The child shall be brought up in an atmosphere which will promote understanding, tolerance and friendship among peoples and national, racial and religious groups and aversion for all forms of national, racial or religious discrimination. He shall be protected from practices based on any such discrimination. He shall be brought up in a spirit of peace, friendship and brotherhood among nations in the consciousness that he will achieve his fullest development and derive greatest satisfaction through devoting his energy and talents to the service of his fellow men, in a spirit of universal brotherhood and peace.

What a wonderful challenge! but this is an age when man is striving physically to move among the heavens. However, let us not neglect the spiritual achievement of heavenly heights while our feet are still upon the earth. A jubilee is not only an opportunity for rejoicing—but should also be an occasion for resolution. As Australia is a signatory to this charter, every one of us in this country is committed to high responsibility. Let each of us examine our conscience and resolve that we will discharge this responsibility to the best of our endeavour. Dr. Billy Graham told us that the most powerful force in the world today is not uranium and the atomic bomb, but youth. Fifty years ago you began your contribution towards ensuring healthy, happy youth. Over the years between you have placed the community increasingly in your debt by your wonderfully successful achievement. But the challenge, though changing, still remains. How dull would life be did there not remain those hills to climb! And "A Call to the People of Australia" inspires us: "Our present dangers are a challenge to us; but in meeting the challenges of history, peoples grow in greatness."

A SIMPLIFIED METHOD FOR THE ENZYME TREATMENT OF ERYTHROCYTES.

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THE use of enzyme-treated cells for the additional sensitivity that they provide in the detection of rhesus antibodies is well established in blood group serology. Trypsin and papain are the enzymes commonly used. The

main disadvantages until now have been the tedious washing necessary to free the cells of enzyme-inactivating substances, and the fact that the enzymes themselves have not been very stable in solution.

It has been shown by various workers (Stratton, 1953; Löw, 1955; Hekker *et alii*, 1957) that it is possible to enhance the activity of the enzyme papain by the use of "activators". Activation overcomes the enzyme-inhibiting effect of serum or plasma, and preliminary washing of the red cells to be sensitized is eliminated. This has so facilitated preparation of these cells as to render their use suitable for routine work.

The activity of the enzyme papain depends on the state of oxidation of the sulphhydryl grouping, oxidation of the –SH– grouping to the –SS– form rendering the enzyme inactive. The amino acid cysteine has been considered the most suitable activator for routine work, although, amongst others, glutathione, B.A.L. (2, 3-dimercaptopropanol), EDTA (ethylene diamino tetra acetic acid) and sodium cyanide have been tested.

Stratton (1953) described a slide test for the detection of antibodies in which cysteine was utilized as an activator, and Löw (1955) and Hekker *et alii* (1957) also made use of it in methods for Rh typing. Stratton's method, although clearly demonstrating the advantages of an "activated" papain solution in testing for antibodies, entails lengthy preparations.

The purpose of this paper is to describe the preparation of enzyme-treated cells for antibody detection by two methods which are considerably simpler than those previously reported. In one method cysteine is used as the activator, and in the other thioglycollic acid. The preparation of a comparatively stable papain solution is also described.

Materials and Methods.

Reagents.

The reagents required are as follows.

1. Buffer solution. Sorenson's phosphate buffer solutions are used—(*a*) 9·47 grammes per 100 ml. of di-sodium monohydrogen phosphate (Na_2HPO_4) and (*b*) 9·08 grammes per 100 ml. of potassium dihydrogen phosphate (KH_2PO_4) are stored separately. Solution (*a*) (7·7 ml.) and solution (*b*) (2·3 ml.) when mixed together will give a solution of pH 7·3, and may be mixed conveniently as required.

2. Buffered saline. Ten millilitres of the mixed buffer solution described above are added to 90 ml. of isotonic saline.

3. Cysteine hydrochloride, 0·5 molar solution. Cysteine is available in the form of L-cysteine hydrochloride (British Drug Houses). This oxidizes slowly and cannot be kept as a stock solution for more than a few weeks. In order to avoid hæmolysis of the blood cells, it is necessary to neutralize the hydrochloride radicle by adding normal (N/1) sodium hydroxide solution, checking the pH with indicator paper. A pH of 7·2 must not be exceeded, as cysteine is precipitated in more alkaline solutions.

4. Thioglycollic acid (British Drug Houses), 10% v/v.

5. Papain solution. One gramme of papain (British Drug Houses) is added to 100 ml. of sterile isotonic saline in a stoppered container. The mixture is shaken vigorously to ensure that as much papain as possible goes into solution. It is cleared by filtration, centrifugation or sedimentation. This solution keeps indefinitely at –20° C., but is unreliable after one week when stored at 2 to 4° C. It deteriorates rapidly at room temperature.

6. Thioglycollic acid – papain stock solution. This consists of isotonic saline, 98·5 ml., thioglycollic acid 10% v/v, 1·5 ml., and papain (British Drug Houses), 1·0 gramme. The mixture is shaken vigorously in a stoppered container for a few seconds and cleared by centrifuging or being allowed to sediment. The pH is 3·3.

7. Red cells. Pooled group O, Rh_o (D) positive cells are collected in acid-citrate dextrose solution and stored at 4° C. Group O, Rh-negative (cde) cells and group O, Rh″ (cdE) cells are stored similarly.

Standard Method for Preparing Papainized Cells.

Previously our standard method for preparing sensitized cells was to make a 2% suspension of washed red cells in buffered isotonic saline (pH 7·3), to which 1% papain had been added. This mixture was incubated at 37° C. for 30 minutes, after which it was centrifuged and the washing of the cells repeated.

Modified Method (I) for Preparing Papainized Cells.

Modification was effected in the first place by incorporating L-cysteine hydrochloride in the buffered saline-papain-red cell mixture. Incubation in a water bath at 37° C. for ten minutes was found to be adequate. After centrifuging, the supernatant was removed and the cells where resuspended in isotonic saline for use. Loss of activity was rapid at room temperature and this pH, and it was necessary to avoid delay in adding the red cells. The composition of the mixture became: buffered saline, 83 ml.; cysteine hydrochloride solution (0·5M; pH adjusted to 7·2 with N/1 sodium hydroxide solution immediately before use), 5 ml.; papain (1% solution), 10 ml.; red cells (unwashed), 2 ml.

Modified Method (II) for Preparing Papainized Cells.

In an endeavour to simplify the test further, other substances capable of acting as reducing agents were investigated. These were ascorbic acid, thioglycollic acid and stannous chloride.

Thioglycollic acid proved much easier to use than cysteine, being more stable in solution, and by careful adjustment of the amount of the acid to be used in the mixture, preliminary neutralization was rendered unnecessary. When the papain solution was acidified initially with thioglycollic acid (solution 6), it was rendered very much more stable, no longer requiring storage at –20° C., and in contrast to the usual saline-papain mixture, which deteriorated rapidly, this solution has been found to retain its activity for five weeks when stored at 4° C. Short periods at room temperature have no detrimental effect, and it is possible to keep it at room temperature for up to five days without very much loss of potency. Full activity may be restored, when necessary, by adding thioglycollic acid once again, provided that care is taken to preserve a suitable pH. The composition of the mixture for the preparation of the cells was now simplified as follows: buffered saline, 88 ml.; thioglycollic acid-papain solution, 10 ml.; packed red cells (unwashed), 2 ml.

TABLE I.

Comparison of Rh Antibody Titres in Serum (Using Papain and Cysteine-Papain Treated Cells).[1]

Sample Number.	Papain.	Cysteine Papain.	Sample Number.	Papain.	Cysteine Papain.
1	64	256	9	256	512
2	64	256	10	4	8
3	16	64	11	64	128
4	64	128	12	256	256
5	2	8	13	4	64
6	128	512	14	16	128
7	64	128	15	128	256
8	128	256			

[1] The figures quoted are the reciprocals of the last dilution in which agglutination occurred, which was visible to the naked eye.

Incubation in a water bath for ten minutes at 37° C. sensitizes the red cells, which, after centrifugation and removal of the supernatant, should be covered with a small amount of isotonic saline. They may then be stored in a refrigerator for up to five days without deterioration.

The use of stannous chloride as the activator showed similar advantages, and will be the subject of further work.

Ascorbic acid proved unsatisfactory.

Screening Test for Antibodies Using Papainized Cells.

A rapid screening test for antibodies similar to that devised by Stratton (1953) is possible with papainized cells.

TABLE II.

Comparison of Sensitivities of Different Techniques for the Detection of Rh Antibodies.

Sample Number.	Coombs Test.	Plasma Albumin.	Activated Papain.	Sample Number.	Coombs Test.	Plasma Albumin.	Activated Papain.
1	–	–	±	11	+	–	++
2	–	±	+++	12	+	±	+++
3	+	±	+++	13	–	±	++
4	+	+	+++	14	–	–	+
5	–	–	++	15	–	–	++
6	+	+++	+++	16	+	+	+
7	–	+	+++	17	–	–	++
8	+	++	+++	18	+	–	+
9	–	+	+++	19	–	±	+++
10	+	++	+++	20	+	+	+++

One drop of the serum under test and one drop of sensitized cells are placed in a small tube or on a slide. Incubation for 10 minutes will usually demonstrate the presence of antibodies of the Rh, P, Lewis and Kell systems.

Cross-Matching Method Using Activated Papain.

For cross-matching using activated papain, a small volume of the sensitizing mixture in the proportion of one part of acidified papain stock solution to nine parts of buffered saline is prepared (1 to 2 ml. will suffice). A few drops of donor's cells, which need not be washed, are added to give a 10% suspension. The mixture is then incubated in a water bath for 10 minutes at 37° C. It is then centrifuged, the supernatant removed, and the cells resuspended in isotonic saline to a suitable concentration. One drop of these cells and one drop of the recipient's serum are incubated in a small tube or on a slide for 30 minutes at 37° C.

Comparison of Standard Papain with Activated Papain.

Serial dilutions in isotonic saline or sera known to contain antibodies were prepared in duplicate. To each tube of one set an equal volume of a 10% suspension of standard papainized cells was added. To the corresponding tubes in the other set an equal volume of a 10% suspension of activated papain treated cells was added. The tests were read after incubation for 30 minutes in a water bath at 37° C.

Technique for Plasma-Albumin Test.

One drop of a plasma-albumin suspension of group O, Rh_o (D) positive red cells and one drop of the serum under test were incubated on a slide in a moist chamber at 37° C. for 30 minutes.

Technique for Indirect Coombs Test.

The indirect Coombs test was performed by adding one part of a 50% suspension of group O, Rh_o (D) positive red cells to five parts of test serum. After incubation at 37° C. for 30 minutes and washing three times with large volumes of saline, the cells were resuspended to a suitable concentration. One drop of this suspension and one drop of Coombs reagent (Commonwealth Serum Laboratories), diluted 1:4, were mixed together on a slide. The tests were read after 10 minutes.

Results.

As will be seen from Table I, in testing for incomplete Rh antibodies, the use of cells treated by activated papain (Method I) provided a much more sensitive titration method than did the use of cells papainized by the standard method.

Cells treated with papain activated by thioglycollic acid (Method II) gave results identical with those obtained with cells treated with the cysteine-activated papain solution.

In the routine testing of ante-natal sera in the Red Cross Blood Transfusion Service (Victorian Division), it has been observed that the presence of antibodies is detected occasionally with papain-treated cells, well before the response to the Coombs test has become positive.

Table II sets out a comparison of the results of tests of a number of sera containing Rh antibodies using the indirect Coombs technique, cells suspended in plasma-albumin and cells treated by activated papain.

Discussion.

The sera referred to in Table II, except for numbers 19 and 20, were taken at random from a stock of samples collected over a period of years, sealed in ampoules and stored at 4° C. In each case the response to the Coombs test was positive when the sample was first collected. The greater sensitivity of the papainized cells is evident in almost every sample, and the method offers a better controlled system than is possible with the complex Coombs test.

Though concerned primarily with the treatment of cells for the detection of Rh antibodies, the method also provides a highly sensitive means of detecting antibodies of certain other blood group systems. We have obtained enhanced reactions for P, Lewis and Kell systems, but Duffy, Lutheran and MNS antibodies have failed to react at all. The method, therefore, is not suitable as a solitary cross-matching test.

Recently an example of anti-e (hr") serum giving a reaction with the Coombs test, and with albumin a result almost too weak to read, produced strong (+++) agglutination when tested with papainized cells.

Summary and Conclusions.

Two techniques for the sensitization of red cells with activated papain have been presented. In Method I, cysteine is the activator; in Method II, thioglycollic acid is used. Both show increased sensitivity as compared with standard methods.

The modifications described have simplified the preparation of sensitized cells so that their use in routine work is practicable even in the smallest laboratory.

Thioglycollic acid is a cheaper and more readily available activator than cysteine, and also permits the preparation of a stable papain solution. It has replaced cysteine in our laboratory.

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Reports of Cases.

A CASE OF CUSHING'S SYNDROME.

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THE clinical features of Cushing's syndrome have been well recognized since Harvey Cushing (1932) first described his cases. Since the introduction into therapeutics of hydrocortisone, cortisone and their subsequent modifications, it has become apparent that prolonged administration of these steroids may produce a condition indistinguishable from Cushing's syndrome. As a result, one looks to the adrenal cortex, rather than to the anterior lobe of the pituitary, for the causal lesion.

The naturally occurring disease is still a rarity, and it is difficult, therefore, to acquire practice in its management. The present case is reported in order to add to the common experience of the syndrome, and to reemphasize some of the problems in diagnosis, treatment, post-operative care and prognosis.

Clinical Record.

Mrs. A. first came under notice in March, 1958, complaining of retrosternal pain on exertion, radiating to the neck, and first noticed after a fall on to the back two weeks before. There was no pain on respiration. The pain was unaffected by meals, although there was some flatulent dyspepsia. At times she had difficulty in swallowing food and fluid—not a sense of obstruction, but one of weakness of the muscles of deglutition. She volunteered that she had been nervy and irritable for a few months. There had been some dyspnœa on exertion, and intermittent cough with yellowish sputum. She had been under treatment for hypertension with "Serpasil" and a reducing diet. Her family history was excellent; both parents were alive, and aged over 80 years.

On examination of the patient, her weight was 74 kg. and her appearance and build were noted as resembling somewhat that of a subject of Cushing's syndrome, although the term was used descriptively and not with any idea of diagnosis. There was slight exophthalmos, but this was not noticed by the patient as varying from her normal appearance. Her blood pressure was 175/110 mm. of mercury, there was splitting of the first heart sound at the apex, and an electrocardiogram showed myocardial ischæmia. The urinary specific gravity was 1·020, and the urine contained no albumin or sugar.

She was admitted to hospital and treated as being threatened with a myocardial infarction, and was discharged after three weeks, clinically improved, with some reversion of the electrocardiogram towards normal. Anticoagulant therapy was continued for a time, but the appearance of petechiæ across the breasts led to suspension of this treatment, although the prothrombin concentration was not below 50%. Her weight was lowered by a continuation of the reducing diet, and some ankle œdema was treated with injections of "Thiomerin". In July, spontaneous bruising was noted on the left forearm. Her blood pressure was 210/110 mm. of mercury. A few purpuric spots were still seen on the breasts and legs. Another electrocardiogram resembled the first taken, with deep inversion of *T* waves in standard lead I and lead *aVL*, and moderate inversion in leads *V*5 and *V*6.

Shortly afterwards, a light fall caused severe dorsal pain, and an X-ray examination revealed compression fractures of the ninth and eleventh thoracic vertebræ without disturbance of the spinal curvature, together with fractures of the left fifth, sixth, ninth and tenth ribs in the posterior axillary line with evidence of callus formation, of the neck of the right twelfth rib, and of the right second and fifth ribs in the anterior axillary line. All osseous tissue was of poor density. A provisional diagnosis of Cushing's syndrome was made. On inquiry, increasing muscular weakness was found to be now present, and some degree of muscle wasting was detectable. An X-ray examination of the skull revealed no abnormality of the pituitary fossa. A glucose tolerance test produced a mildly diabetic type of curve.

The patient was admitted to the St. George Hospital for further investigation and treatment. Positive clinical findings, at this time, were as follows: (i) centripetal obesity; its degree, but not its distribution, had been modified by a low-calorie diet; (ii) plethoric complexion; (iii) facial hirsuties; (iv) scattered small ecchymoses; (v) muscle weakness and wasting; (vi) hypertension; (vii) a mildly diabetic type of glucose tolerance curve; (viii) multiple fractures with generalized osteoporosis. Laboratory investigations gave the following information. The serum electrolyte concentrations were as indicated in Table I. These did not show the hypokalæmic, hypochloræmic alkalosis described in some cases. Cope and Raker (1955) found a low serum potassium level in 9% of their series, and a high serum carbon dioxide content in 37 of 43 cases in which it was tested. The serum calcium and phosphorus contents were also estimated, with the following results: serum phosphorus content (as inorganic phosphate), 3·8 mg. per 100 ml.; serum calcium content, 9·5 mg. per 100 ml. The hæmoglobin value was 16·8 mg. per 100 ml. A white cell count revealed 9500 leucocytes per cubic millimetre, only 8% being lymphocytes; no eosinophils were present. Excretion urography gave no indication of any suprarenal tumour. Estimations of steroid contents of the blood and urine were carried out by Dr. A. W. Steinbeck, of the Medical Professorial Unit, University of Queensland. The findings after an infusion of 25 units of ACTH are shown in Table II. These confirmed the diagnosis of Cushing's syndrome. Unfortunately, it had not been possible to send a sample of urine collected before the ACTH administration, so that prediction of the nature of the adrenal lesion was not practicable.

In view of the negative urographic findings, it seemed likely that bilateral hyperplasia was the most probable cause. Bilateral total adrenalectomy was decided upon, and the left adrenal was removed on October 14. Hormonal cover was ordered according to the scale in use at the hospital for adrenalectomy (see Table IV). At operation, the left adrenal was exposed through a lumbar incision. No gross abnormality was found on exposure of the gland *in situ*. Shortly after ligation of the adrenal vein, the anæsthetist reported a fall in blood pressure, which he was able to control satisfactorily during division of the adrenal arteries and removal of the gland.

In the immediate post-operative period, in spite of the liberal premedication with cortisone, the patient had a severe reaction and became markedly hypotensive. The blood pressure was maintained by an intravenous infusion containing "Neo-synephrin". An attempt to use noradrenaline induced angina and had to be abandoned. After a stormy 48 hours, during which time 250 mg. of cortisone were given every four hours, the patient settled down into a more comfortable state. The onset of congestive cardiac failure, a few days later, was attributable to DOCA, and settled down quickly when this was suspended.

The pathological report on the gland described it as of normal size. Microscopically, the adrenal was not grossly abnormal. There was an occasional island of cellular hypertrophy with some periadrenal fibrosis.

On October 28, the right adrenal was removed. This time, in view of the high dosage needed on the first occasion, the cortisone cover was as shown in Table III, with a potassium supplement beginning on the fourth post-operative day. The course after operation lacked the stormy features of that following the first adrenalectomy.

At operation, the right adrenal was exposed through a lumbar incision, and a spherical tumour was at once noticed on palpation and inspection of the gland. However, the relatively small size of the tumour and of the gland as a whole facilitated its removal, which did not present any technical difficulties. The pathologist reported that the adrenal was macroscopically of half the normal size, partly replaced by a variegated yellowish tumour 1·4 in.

TABLE I.

Date.	Sodium (Na+) (mEq./l.).	Potassium (K+) (mEq./l.).	Chloride (Cl−) (mEq./l.).	Carbon Dioxide Combining Power (HCO_3−) (mEq./l.).	Protein. (Grammes per 100 ml. of Serum.)	Specific Gravity of Plasma.
23. 9.58	136	4·4	100·9	29·9	6·5	1026
17.10.58	138	3·8	97·0	—	6·5	1026
23.10.58	140	3·0	103·8	—	5·8	1026
7. 1.59	142	5·0	103·2	28·3	6·5	1026

in diameter. Microscopically, the tumour showed the structure of a carcinoma of the adrenal cortex. It appeared to be of low-grade malignancy.

The amount of cortisone was gradually reduced, so that the dose was 75 mg. per day by the tenth day. At this point, a brief febrile episode associated with wound infection occurred, necessitating raising the dosage to 200 mg. per day for two days, 150 mg. on the succeeding day, then 100 mg. per day for five days, and finally back again to 75 mg. per day. On this dose, the patient was discharged from hospital on November 17. By the end of the month, the daily dose was 50 mg., and by December 9, 37·5 mg. It was thought that the longer a high maintenance dose was used, the slower would be the recovery of the osteoporosis. Persistence of ankle œdema led to the

TABLE II.

Measurement.	17-Ketosteroids. (Mg. in 24 Hours.)	17-Ketogenic Steroids. (Mg. in 24 Hours.)	17-Hydroxycorticosteroids.	Steroidal Dihydroxyacetones. (Mg. in 24 Hours.)
Urinary excretion rate:				
12.10.58 ..	16·6	31·9	35·1 mg. in 24 hours	16·1
20. 1.59 ..	1·3–1·6	25·0	25·0 mg. in 24 hours	—
Plasma concentration (Porter and Silber)	—	—	58 µg. per 100 ml.	—

administration of mersalyl and stopping of the sodium chloride supplement. The patient was stronger and was walking about; her weight was 68 kg. and her blood pressure 150/100 mm. of mercury, and an electrocardiogram showed slight *S–T* depression in leads I and *aVL*, but upright *T* waves in all leads except *aVR*. Her peripheral arteries caused concern, no pulsation being detected in the posterior tibial and dorsalis pedis arteries. Dermatitis of the axillæ and groins developed, and a series of small furuncles in the axillæ and groins and some styes supervened. At the same time, anorexia, nausea, headache and a blood pressure reading of 120/90 mm. of mercury suggested the need for more cortisone. This was increased to 75 mg. per day. It was found necessary to continue this dose for two weeks.

On January 7, 1959, her weight was 68 kg. The serum electrolyte concentrations were as shown in Table I, and the blood pressure was 145/95 mm. of mercury. Staphylococcal lesions of minor type occurred until tetracycline was used. Flexural eczema was troublesome in a recurrent fashion, but responded to fludrocortisone ointment; rheumatic pains in wrists and fingers, not relieved by phenylbutazone, developed, and these have continued to worry the patient. Further sudden pains in the back suggested that the osteoporosis was not decreasing and that damage was continuing there. An X-ray examination of the spine showed compression fractures of all the thoracic vertebræ from the fourth downwards, and of the first and second lumbar vertebræ. These compressions were mainly at the expense of the superior surfaces of the vertebral bodies, but the inferior surfaces were also involved and many of the vertebræ were biconcave. A marked degree of osteoporosis was present. Therefore, on February 3, 25 mg. of "Durabolin" were injected intramuscularly, and this injection was repeated weekly thereafter in an attempt to accelerate the reconstitution of bone. A back support was fitted, and the dose of cortisone was reduced to 37·5 mg. per day. The patient now lost her back pain and felt better than she had done for over a year.

Further plasma steroid estimations on January 20 had given the results shown in Table II. At that time, the average daily dosage of cortisone was 62·5 mg. per day. Dr. Steinbeck commented that a 24 hour excretion of 25 mg. of ketogenic steroid would be within the normal range for a daily ingestion of 50 mg. of cortisone. On February 23, a glucose tolerance test gave a normal curve.

TABLE III.

Cortisone Cover for Second Adrenalectomy.

Day.[1]	Cortisone. (Milligrammes.)
D−2	300
D−1	500
D	1500
D+1	1200
D+2	600
D+3	400
D+4	200
D+5	200
D+6	200
D+7	200
D+8	100

[1] "D"=day of operation; "D−", before operation; "D+", after operation.

The patient is now fairly active and able to work, and feels energetic. Her blood pressure is in the range 145-150/90-100 mm. of mercury. Increase of the jugular venous pressure occurs easily with exertion, and it is thought that the cardiac reserve is not great. However, an electrocardiogram on March 23 showed a considerable return to normal. Hirsuties have diminished. Falling scalp hair has been noted for several months, and the process is still present; but new hair appears to be growing. She understands the need to increase the cortisone dosage for certain emergencies — infection, trauma, operation, etc. There is no evidence of any recurrence of her lesion.

Discussion.

This patient showed the manifestations of severe Cushing's syndrome. The speed with which osteoporosis and muscle weakness became disabling led to the belief that exploration would provide the quickest solution to the problems of ætiological diagnosis and treatment, and, indeed, it is not yet possible reliably to exclude adrenal tumour by any means short of surgical exploration according to Montgomery and Welbourn (1957). Presacral air insufflation was not attempted. In a subsequent case of adrenocortical secretory tumour, it proved of value in indicating the side of the lesion, and it should have been attempted in the present case. Had the right adrenal been explored first, bilateral adrenalectomy would have been avoided. It is commonly stated that adrenocortical tumours are more frequent on the right side; however, Macfarlane (1958) reported that of 55 carcinomata, secretory and non-secretary, of the adrenal cortex, 31 were

on the left and 24 on the right side. It is thus a matter of debate which adrenal should be explored first. It was considered that bilateral hyperplasia was the most likely causal lesion, and that the need to terminate the disease process as quickly as possible, in view of the advancing bony damage, made total adrenalectomy the operation of choice. Subtotal operations for bilateral hyperplasia are often successful and are preferred by many surgeons. Although often avoiding the need for permanent cortisone therapy and the risks of sudden changes of cortisone requirements, they are uncertain in their effects. Removal of insufficient tissue allows the disease process to advance and requires a further operation. On the other hand, in experimental animals, atrophy of the remaining fragment of gland has occurred, according to Glenn *et alii* (1958), who favour total adrenalectomy. Welbourn (1958) found that of 10 patients surviving 10 months or more after subtotal adrenalectomy, five required no cortisone, four had had to take it again, and one had not been able to do without it at all after operation.

The adjustment of cortisone cover for the operation gave some trouble. Thorn *et alii* (1956) sugegsted the following schedule of hormonal substitution ("D" referring to the day of operation):

D	400 mg. per day
D + 1	300 mg. per day
D + 2	200 mg. per day
D + 3	175 mg. per day
D + 4	150 mg. per day
D + 5	125 mg. per day
D + 6	100 mg. per day
D + 7	100 mg. per day

The dose is further gradually reduced over the ensuing few weeks.

Welbourne (1958) recommends the following dosage:

D − 2	200 mg. per day
D − 1	200 mg. per day
D	200 mg. per day
D + 1 to D + 5	100 mg. per day

Thereafter, a gradual reduction is made over a period of weeks.

Table IV shows the scale in use at the St. George Hospital.

TABLE IV.

Day.	Cortisone.	DOCA.
D−1	50 mg. every six hours.	5 mg.
D	150 mg. before operation. 50 mg. every four hours after operation.	5 mg.
D+1	50 mg. every six hours.	5 mg.
D+2	50 mg. every eight hours.	3 mg. (if necessary)
D+3	50 mg. every 12 hours.	—
D+4	25 mg. every eight hours.	—
D+5 to D+7 ..	25 mg. every 12 hours.	—

Cortisone is given orally after the fourth post-operative day.

Cortisone is given orally after the fourth post-operative day.

In the present case, these doses were exceeded many times on the day of operation and for several days after, since standard dosage proved insufficient to avoid a severe hypotensive crisis. The amended scale, shown in Table III, was used for the second operation, and the course was smooth. Apparently, the intensity of the disease process varies from mild to severe and requires corresponding variation in the hormonal cover. It is safer to be too liberal than too niggardly. As far as DOCA is concerned, it is considered advisable to discontinue its routine use in this schedule, since it adds to the risk of congestive cardiac failure.

The establishment of a final maintenance dose of cortisone is a time-consuming affair in which considerable attention to detail is needed. If the daily intake is lowered too rapidly, fatigue, anorexia, nausea and hypotension develop. On the other hand, maintenance of high dosage for too long permits increase in osteoporosis, further pathological fractures and worsening pain. By the weekly injection of "Durabolin", it was hoped to accelerate the recovery of normal bony strength without virilizing side effects. It is not possible to state whether any such effect was produced, although clinical improvement occurred from that time onwards, since the patient's back support was finally fitted and the dose of cortisone reduced at the same time as the "Durabolin" injections were begun. The rapidity of progression of bony damage is exemplified, in this case, by comparison of pre-operative and post-operative X-ray films of the spine. That this is probably not due to functioning metastases is suggested by the progressive gain in strength and well-being, the more normal electrocardiogram, a glucose tolerance curve in the low range of normal, normal figures for urinary steroid excretion three months after operation, and the fact that reduction of cortisone dosage below a certain level causes symptoms of adrenal insufficiency.

Exophthalmos was reported by Cushing (1932) in a few cases, and by Plotz *et alii* (1952) in 6% of their own series and 8% of previously reported cases. Morgan and Mason (1958) report a case in which the onset of malignant exophthalmos preceded that of the main syndrome. In our case there was slight proptosis, which has receded since operation.

The nervous irritability, noted at the time of the patient's admission to hospital, is a common finding. Depression is still more common, and the suicide rate in the series reported by Starr (1952), was 1000 times that in the general population.

The absence of pulsation in the posterior tibial and dorsalis pedis arteries is not at present accompanied by any symptoms. The significance of Cushing's syndrome, as the ætiological factor in this patient's arterial disease, is underlined by the excellence of her family history. It is hoped that the improvement in the coronary circulation, as shown in the electrocardiogram and her effort tolerance, can be duplicated in the circulation of the lower limbs. Apart from the risks of local recurrence of her lesion or of metastases, and of episodes of adrenal insufficiency, the hazards of coronary and peripheral vascular occlusion are the biggest threat to the patient's continued well-being.

Finally, it should be emphasized that the handling of this case has been effected by team work between physician, surgeon, anæsthetist and laboratory services. Such cooperation is particularly necessary in the period immediately after operation, when errors of judgement and delays or mistakes in therapy can be rapidly disastrous.

Summary.

A case of Cushing's syndrome, occurring in an adult female, is reported.

The diagnosis and further management are discussed.

Acknowledgement.

We wish to thank Dr. A. W. Steinbeck, of the Medical Professorial Unit of the University of Queensland, who carried out the steroid estimations.

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CONGENITAL METHÆMOGLOBINÆMIA.

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Cyanosis in the new-born always demands diagnosis and treatment. Since in the majority of cases heart or lung disease is responsible, cyanosis from other causes may be misdiagnosed unless full investigation is performed.

In the present case, neonatal cyanosis was due to methæmoglobinæmia—not the well-recognized form due to chemical contact, but that due to a rare inherited defect of metabolism. This is the seventh case in which the diagnosis has been made in an infant, and is the first case of congenital methæmoglobinæmia reported in Australia.

Clinical Record.

A male baby, aged 17 days, was admitted to the Royal Children's Hospital, Melbourne, with a diagnosis of congenital heart disease, as he had been cyanosed since birth. His mother's pregnancy and labour had been uneventful, though delivery occurred two weeks prematurely. The child had gained weight on breast feeding, but remained a grey-blue colour despite the administration of oxygen. His birth weight was 5 lb. 7 oz. The child's parents are healthy, but are first cousins (Figure I); a brother, aged two years, is quite normal, and there is no family history of cyanosis. No contact with unusual drugs or chemicals could be traced.

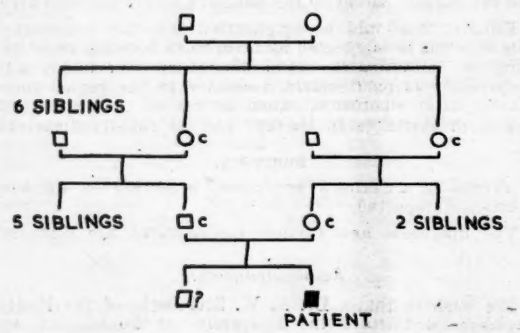

Figure I.

Siblings as shown reported to be normal. Open squares, males; open circles, females; "c" carrier; "?" possible carrier.

The baby appeared normal apart from central cyanosis; investigation of his heart by X-ray examination of the chest and electrocardiography showed no abnormality, and the hæmoglobin value was 15·4 grammes per 100 ml, the leucocyte count being 7000 per cubic millimetre.

[1] Present address: Royal Melbourne Hospital, Melbourne.

Although at this stage he was considered to have a congenital cardiac defect, his venous blood was very dark, and was shown on spectroscopic examination to contain methæmoglobin, even in high dilution. (Unfortunately no quantitative analysis was performed at this stage.) As a final test, 25 mg. of methylene blue as a 1% aqueous solution was given orally, and within one hour the child was pink.

Ascorbic acid has been given daily since the time of diagnosis. Up to the age of four months he was given 100 mg. per day, but some cyanosis reappeared, and he has since received 300 mg. per day. This has caused no ill effects, and he is almost free from cyanosis. On rare occasions when cyanosis has been obvious his parents have given him a single dose of 25 mg. of methylene blue by mouth.

During the ten months that the child was in our care, his development appeared normal; by nine months he was able to sit up and play with blocks, and to move about on his buttocks; by 10 months he was crawling and standing with support, and he weighed 25 lb.

With ascorbic acid treatment cyanosis is barely detectable, and on several occasions the methæmoglobin content was estimated at 12% or 14% of the total hæmoglobin content. After 25 mg. of methylene blue had been given orally, this percentage fell from 12 to zero within an hour.

The blood groups of the family have been tested and are shown in Table I. Unfortunately the basic enzyme defect could not be investigated; but it was found that the methæmoglobin level of heparinized venous blood stayed constant on incubation with glucose at 37° C. for four hours—thus differing from drug-induced methæmoglobin.

The possibility that all his methæmoglobin was fœtal methæmoglobin was discounted, when in the same blood sample methæmoglobin was 12% and fœtal hæmoglobin 6·7% of the total hæmoglobin.

Discussion.

While methæmoglobinæmia due to ingestion of sulphonamides, nitrates and nitrites, or to contact with aniline dyes, is widely known, this condition is rarely encountered as a congenital and persisting abnormality.

Some 100 cases have been reported, mainly since the paper by Barcroft *et alii* (1945). The condition is more easily followed in closed communities, and Codounis has published two family trees showing inheritance through several generations in Greek families.

This is the seventh case of congenital methæmoglobinæmia identified and treated in infancy, previous cases having been reported by Korver (1953), by Gasul *et alii* (1952), by Dine (1956) and by Lees and Jolly (1957). The case reported by Schwartz and Rector (1940) must be excluded, as methæmoglobinæmia disappeared permanently after the child received one dose of methylene blue.

The inheritance of methæmoglobinæmia is debated; evidence points in some cases to a dominant trait (Baltzan and Surgarman, 1950) and in others to recessive inheritance (Codounis, 1952; Gibson and Harrison, 1947; Breakey *et alii*, 1951). The present case is the only reported instance of a cousin marriage with affected children, and although other members of the family cannot be examined, this strongly suggests recessive inheritance. It is likely that different modes of inheritance do occur, possibly with different biochemical defects responsible for the presence of methæmoglobin.

Although according to Mendelian laws the children of this family should be one affected, two carriers and one unaffected, it has been impossible to decide whether the brother carries the trait. Spectroscopic examination of his blood, and of that of the parents (who must be carriers unless a mutation has occurred) revealed no methæmoglobin.

This child has developed normally both mentally and physically up to the age of 10 months: this supports the suggestion of Worster-Drought *et alii* (1953) that mental

TABLE I.

Subject.[1]	A-B-O.	MNS.	Rh.	P.	Le^a.	Fy^a.	K.	Lu^a.	Wr^a.
Patient ..	A_1	MNS	Rh_1Rh_1	+	−	+	−	−	−
Brother	O	MNS	Rh_1Rh_1	+	−	+	−	−	−
Father ..	O	MNS	Rh_1Rh_1	+	−	+	−	−	−
Mother	A_1	MS	Rh_1Rh_1	+	+	+	−	−	−

[1] All four blood samples gave negative results with anti-rh^w (C^w) and with anti-Gr.

deficiency accompanying congenital methæmoglobinæmia is due to another genetic defect which is separately inherited.

The best account of investigation of the enzyme defect responsible for congenital methæmoglobinæmia is that of Gibson (1948). It has been shown that methæmoglobin is constantly formed in small amounts in the blood by oxidation of hæmoglobin iron to the ferric form. In normal people this is removed by a reduction system including coenzyme 1 and diaphorase 1, but in congenital methæmoglobinæmia diaphorase 1 activity is reduced, and methæmoglobin accumulates to a new level of equilibrium.

There are two forms of treatment available; ascorbic acid acts slowly as a direct reducing agent when significant blood levels are reached, while methylene blue is effective in small amounts, by catalyzing a second reduction system which normally acts only slowly to reduce methæmoglobin.

Summary.

Congenital methæmoglobinæmia has been diagnosed in a child aged one month, and treatment by ascorbic acid and methylene blue has been effective.

Since his parents are first cousins, it is strongly suggested that this disease is due to homozygous inheritance of a recessive trait.

Spectroscopic examination of blood can quickly distinguish methæmoglobinæmia from the more common cardiac and pulmonary causes of cyanosis in the new-born.

Acknowledgements.

I wish to thank Dr. H. E. Williams for allowing me to report this case, and also Mr. I. C. Parsons of the Peter MacCallum Clinic, and Mr. R. T. Simmonds of the Commonwealth Serum Laboratories, Melbourne, for their help with biochemical tests and blood grouping.

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Reviews.

Applied Pharmacology (Clark). By Andrew Wilson, M.D., Ph.D., F.R.F.P.S., and H. O. Schild, M.D., Ph.D., D.Sc.; ninth edition; 1959. London: J. & A. Churchill Limited. 8½" × 5½", pp. 760, with 165 illustrations. Price: 50s. (English).

IT is very pleasing to see a new edition of "Clark", since it has become probably the most useful textbook of pharmacology in small compass. This edition fills a very real need, since new drugs are introduced so frequently—and some are really quite useful—that pharmacological textbooks date extremely quickly, and the best of them when three years old can hardly be recommended to the student. Up-to-dateness often has to replace quality in this case. Professor Wilson and Dr. Schild have maintained the standard they have set in the earlier edition and present the pharmacology of a very complete range of drugs with great clarity. They emphasize the pharmacological basis of therapy, and do not delve appreciably into esoteric laboratory experiments. This is important, because the professional pharmacologist is rightly more interested in the drugs themselves than in their therapeutics, whereas the medical student, for whom this book is intended, must understand the basic pharmacology for his future application.

Each chapter is a model of concise and clear writing, and concludes with a list of the official preparations of the drugs discussed and a collection of selected articles for further reference. It would be pointless to indicate the coverage of the book, because it is quite complete for the practitioner or student.

The book has been thoroughly reedited, and much new material has been included. There is a very good account of the pharmacology of the central nervous system and the methods which can be used to assess drugs of possible value in psychiatry. The clinical trial and variability of human observations are very well discussed—to pick on only two chapters from others which deserve similar comment.

This book is the best account of pharmacology for the medical student, and it ought to be bought by every general practitioner who needs a concise and reliable account of any aspect of drug therapy.

Pharmacology. By J. H. Gaddum, M.R.C.S., L.R.C.P., Sc.D., F.R.S.; fifth edition; 1959. London, New York and Toronto: Oxford University Press. 8½" × 5", pp. 604, with illustrations. Price: 68s.

THIS popular textbook now appears in its fifth edition. It is written as a textbook for medical students, but is an attempt to present pharmacology less from the therapeutic standpoint, and to include some of the experimental background which lies at the basis of modern therapeutics.

The arrangement of this book is somewhat different from that of most other books on pharmacology, since, although the drugs are grouped in chapters according to their type or their mode of action, there is less restriction in this arrangement than is usual. One chapter, for example, is entitled "Drugs which Destroy Life", and includes a discussion of poisoning and its treatment in man, insecticides and insect repellents, disinfectants and bactericides, and while discussing iodine, the author deals with the radio-opaque substances which contain this element.

The last chapter, dealing with general pharmacology, contains a great deal of valuable information rarely to be found so clearly presented. It discusses the principles of biological assay, the design of therapeutic trials, toxicity testing and the elements of the statistical analysis of biological data. These are fields in which Professor Gaddum has been particularly interested, and this chapter gives all the information necessary to whet the appetite of the investigator or to dampen the enthusiasm of those

who would attempt to place too much reliance on too little experimental evidence.

There are very few drugs which are not mentioned somewhere in the 22 chapters which make up this book, and the author is to be congratulated in dealing with them all in a comparatively small volume.

An innovation in this edition is the inclusion of the doses for all official drugs and many others, and the metric system is used throughout, since this has been almost universally adopted in medical schools today. The only criticism that can be made is that some drugs, not particularly important ones, are dealt with very briefly; but the emphasis is on the experimental basis and the greater interest this gives more than justify the economy of space for drugs which can better be read about elsewhere.

This book is an excellent student textbook of pharmacology, but rather less suitable than some others as a reference book for the practitioner—which, in any case, is not its avowed purpose.

Smoking and Lung Cancer. By *T. W. Lees, M.D.; 1959.* Lanarkshire: T. W. Lees (Publisher). 8½" × 5½", pp. 32, with illustrations. Price not stated.

THE author is dissatisfied with the conclusions drawn by Doll and Hill and by others that relate cancer of the lung and cigarette smoking. He deals with many factors that could invalidate comparisons between cases and controls. His main thesis is that there is "a non-causative correlation between the social habits pertaining to good health (such as smoking and drinking alcohol) and the incidence of certified acute disease".

The Degenerative Back and Its Differential Diagnosis. By *P. R. M. J. Hanraets, M.D.; 1959.* Amsterdam, London, New York, Princeton: Elsevier Publishing Company. 8¾" × 6", pp. 700, with many illustrations. Price: £5 5s.

THE author begins this book with a statement of the problems associated with pain in the lower part of the back and pain of lumbar and sacral root distribution. In the development of the investigation he infers that all low-back pain, as well as radicular pain, is due to involvement of the nerve root. That this is not always due to an intervertebral disk lesion has become more widely realized in the past few years.

The theory put forward is that low-back pain and the radicular syndrome are due to structural weaknesses in the spinal column, its muscles, ligaments, intervertebral disks, etc., and the first portion of the volume is devoted to a detailed exposition of all the various abnormalities which may produce the "weak back". Discussion ranges over many interesting conditions, which include relative stenosis of the vertebral canal on the one hand and manifestations attributed to an excessively wide dural sac on the other, while the numerous anomalies of nerve roots are elaborated in detail.

Against this background of structural abnormality the author discusses constitutional factors and the significance of abnormal movements in relation to the production of symptoms in the degenerative or weak back.

The symptomatology and differential diagnosis are treated in a very exhaustive manner. This portion of the book contains much interesting and useful material; but much of the important information tends to be dispersed amongst too many references and conflicting opinions. At times the subject matter seems hardly relevant to the development of the argument. Neurological signs are discussed at length and accompanied by a statistical study.

The various investigations now currently employed are discussed, and the author's insistence on lumbar puncture before operation is noted. The section on radiological examination comprises an extensive survey of the literature on many of the controversial aspects, largely related to the validity of certain findings, such as narrowing of the disk spaces and abnormalities observed during myelography. With regard to the latter, the author concludes that it is least reliable when it is most needed and should be used only when there are special indications; as set out, these appear very reasonable.

After some philosophical remarks upon the pathogenesis of back pain and some interesting arguments related to compensation for injury, the author concludes with a discussion upon management. All the varied forms of treatment are discussed. An interesting feature of this portion is the description of what the author terms the overhaul operation.

There is much of interest and instruction in this volume, which is a fine example of the publisher's craft. Fine paper and good type and arrangement are supported by excellent illustrations. A feature of the book is the fine line drawings, which are of small size but of great clarity. The few colour plates are of high quality, and the reproductions of radiographs are usually clear, though of small size. Although at times diffuse and discursive, the book has much to recommend it to all who are interested in this subject.

Statistical Methods in Biology. By Norman T. J. Bailey, M.A., D.Sc., 1959. London: The English Universities Press, Limited. 8½" × 5½", pp. 212. Price: 46s. 6d.

THIS is an elementary book by the Reader in Biometry at the University of Oxford. The common statistical problems of the systematization of observations, the estimation of parameters and the testing of hypotheses are treated briefly with the aid of specific examples having a biological flavour. Association and correlation are treated rather better than is usual in an elementary text. There are then some simple examples of the analysis of variance and regression analysis, some hints on computing, a group of statistical tables and a summary. The reader may thus turn up any test rapidly in the summary in order to assist his memory. This book seems to fulfil its limited aims better than any similar book in the field, for the simplified treatment is not gained at the expense of accuracy. Minor criticisms might be the occasional odd mixture of scientific English and slang and the inclusion of the example at the beginning of Chapter 4. The book can be warmly recommended for medical libraries and research workers.

Books Received.

[*The mention of a book in this column does not imply that no review will appear in a subsequent issue.*]

"Cinefluorography: Proceedings of the First Annual *Symposium on Cinefluorography*, Sponsored by the Department of Radiology, University of Rochester, School of Medicine and Dentistry, Rochester, New York, Friday and Saturday, November 14 and 15, 1958", edited by G. H. S. Ramsay, M.D., J. S. Watson Jr., M.D., T. A. Tristan, M.D., S. Weinberg, and W. S. Cornwell, M.A.; 1960. Oxford: Blackwell Scientific Publications Ltd. Springfield: Charles C. Thomas. 9¾" × 6¾", pp. 282, with many illustrations. Price: 94s. (English).

"Effect of Radiation on Human Heredity: Investigations of Areas of High Natural Radiation", First Report of the Expert Committee on Radiation. World Health Organization Technical Report Series, Number 166; 1959. Geneva: World Health Organization. 9¼" × 6¼", pp. 48, with illustrations. Price: 1s. 9d. (English).

"Pressure Group Politics: The Case of the British Medical Association", by H. Eckstein; 1960. London: George Allen and Unwin Ltd. 8½" × 5½", pp. 168. Price: 16s. (English).

"Physiology of the Retina and the Visual Pathway", by G. S. Brindley, M.A., M.D.; 1960. London: Edward Arnold (Publishers) Ltd. 8½" × 5½", pp. 310, with illustrations. Price: 35s. (English).

"Psychiatric Services and Architecture", by A. Baker, R. Llewelyn Davies and P. Sivadon; 1959. Geneva: World Health Organization. 8½" × 5½", pp. 60, with illustrations. Price not stated.

Einrichtung und Methoden des klinischen Laboratoriums", by Eberhard Goetze; 1959. Jena: Veb Gustav Fischer Verlag. Sydney: Angus & Robertson Limited. 9½" × 6¾", pp. 256, with illustrations. Price not stated.

"Nebenschilddrüseninsuffizienz und tetanisches Syndrom", by Jochen Quandt and Werner Ponsold; 1959. Jena: Veb Gustav Fischer Verlag. Sydney: Angus & Robertson Limited. 8½" × 5¾", pp. 184, with 36 illustrations and 2 tables. Price not stated.

"The Hydrogen Ion Concentration in Arterial Blood: A Clinical Study of Patients with Diabetes Mellitus and Diseases of the Kidneys, Lungs, and Heart", by B. Moller; Acta Medica Scandinavica Supplementum 348; 1959. Stockholm: Acta Medica Scandinavica. 9½" × 6¾", pp. 340, with illustrations. Price not stated.

The Medical Journal of Australia

SATURDAY, APRIL 30, 1960.

TUMOUR CELLS IN THE BLOOD.

It has long been assumed that tumour metastases grow from malignant cells transported in the blood-stream, but it is only during the last few years that techniques have been perfected whereby tumour cells in the blood can be fairly readily found and identified. The immediate result of this advance was to demonstrate that, in the presence of many kinds of malignant disease, tumour cells appear in the blood-stream far more frequently and in far greater numbers than most people had probably suspected. The subject has recently been reviewed by I. Salgado, of Montreal, and his colleagues[1] in an article in which they report the results of the examination of blood samples from 100 patients. Thirty of these patients were suffering from non-malignant conditions, and in their blood no abnormal cells which might be confused with tumour cells were found. The other 70 were suffering from cancers of various types. In 10 cases blood was drawn from a vein draining the tumour site, and in four of these samples tumour cells were identified. In the remaining 60 cases peripheral blood was investigated, and in 34 of these tumour cells were recovered. In each case the sample consisted of 15 to 20 ml. of blood. The largest single group consisted of 32 patients with breast carcinoma. In this group, tumour cells were found in the blood post-operatively in five out of 15 cases in which no axillary lymph-node involvement was discovered, in six out of nine cases in which the axillary lymph nodes were involved, but in only two out of eight cases in which generalized metastases were present. In five cases blood samples were taken both before and after operation. Tumour cells were found in none of the pre-operative samples, but in three of the five post-operative samples, findings which support the view that tumour cells are likely to be shed into the blood-stream during operative manipulation; however, some other investigations do not support this conclusion. In one patient tumour cells were still present in the peripheral blood nine days after radical mastectomy.

In general the findings of Salgado and his colleagues are in agreement with those of other workers. There is considerable unanimity on the point that the examination of blood samples for tumour cells is singularly unhelpful as regards the prognosis in individual cases, though these investigations are of great value for the light they throw on the natural history of tumours. Most workers report the finding of tumour cells in blood in between 40% and 50% of cancer patients examined, and this seems to apply to a wide variety of tumours. H. C. Engell of Copenhagen, one of the pioneers in this work, has published the results of a follow-up study[2] of 125 cancer patients whose blood had been examined for tumour cells at operation five to nine years previously. All but ten of the patients in this series had cancer of the rectum, colon or stomach. Whenever possible, Engell took three samples of blood, one from a vein draining the tumour area as soon as the tumour was exposed and before any manipulation took place, a similar one after dissection of the tumour and before ligation of the last vein, and one from an antecubital vein at the same time as the second. His samples averaged 5 ml. in amount. One result of this method was the demonstration that tumour cells were found just as frequently before as after dissection of the tumour in veins draining the area; very few cells were found in the samples of peripheral blood. In only one case in the whole series did operative manipulation produce a considerable outflow of tumour cells, and this was in one of the four cases of carcinoma of the lung included in the series. Another important finding was that the frequency with which tumour cells were found in the blood was directly related to the degree of histological differentiation, using Broder's criteria; thus tumour cells were found in association with 17 out of 50 Grade II tumours, in 48 out of 63 Grade III tumours, and in 11 out of 11 Grade IV tumours. There was a lesser degree of correlation between the frequency of the presence of tumour cells and the local extent of the growth. Of the original 125 patients, 55 were still alive five to nine years later, and 28 of these were among the 76 in whose blood tumour cells were found at the time of operation. This appears to be conclusive proof that the presence of tumour cells in the blood at the time of operation is of no prognostic significance.

Another important paper on the subject is that by J. C. Pruitt, A. W. Hilberg and R. F. Kaiser.[3] These authors developed a method which enabled them to examine quantitatively up to 20 ml. of blood in each sample. (Broadly speaking, all techniques appear to consist of preliminary lysis of the erythrocytes, followed by separation and concentration of the remaining cells by various means.) Using this method, they examined the large number of 300 specimens of peripheral blood, 200 from presumably well people with no evidence and no history of cancer, and 100 from cancer patients. Such a large control series enabled these workers to make some interesting observations on the numbers and variety of unusual cell types to be found in the blood of healthy people, and to establish convincingly that the "tumour cells" were in fact the products of malignant growth. Out of the 200 control subjects the blood from only one contained cells which were considered to be cytologically malignant, and cells from one other subject were considered suspicious. Detailed investigation failed to find any other evidence of

[1] *Canad. med. Ass. J.*, 1959, 81: 619 (October 15).

[2] *Ann. Surg.*, 1959, 149: 457 (April).

[3] *New Engl. J. Med.*, 1958, 259: 1161 (December 11).

cancer in either of these subjects, but it was recommended that they should be reexamined periodically. Out of the 100 cancer patients cells considered to be definitely malignant were found in the blood of 39, and cells considered suspicious in that of 12 others. No suspicious cells were found in the remaining 49 samples. Pruitt and his colleagues conclude that malignant cells are not present in sufficient numbers to justify examination of peripheral blood to make a primary diagnosis of cancer, except in suspected cases that have eluded diagnosis by other means. They suggest that in some cases this technique may be of value to indicate the presence of unsuspected metastases in patients being followed up after operation.

As Pruitt and his colleagues point out, one result of these investigations is the demonstration that a high percentage of patients with cancer have malignant cells which appear to be viable circulating in the blood-stream. A corollary of this is that of all such cells only a very small proportion ever become established. It also makes clear why subtle changes in the patient's internal environment may result in the sudden development of metastases—as sometimes appears to happen after surgical intervention (K. W. Starr *et alii*[4]). The fact that these cells persist in the blood-stream for some time after the removal of the primary growth demonstrates that they have no difficulty in passing repeatedly through the peripheral capillary network, the lungs, and in some cases, the liver. This all lends point to the proposal of G. W. Watson and R. L. Turner[5] to make a trial of combined surgery and cytotoxic chemotherapy in the treatment of carcinoma of the breast; it would seem logical to employ a cytotoxic agent to deal with the tumour cells in the blood while the surgeon attends to the primary growth and its immediate neighbourhood. A large scale cooperative study, involving 48 departments of surgery, is in fact in progress in the United States under the auspices of the National Cancer Institute with the object of investigating the adjuvant use of chemotherapy in the surgical treatment of cancer (M. B. Shimkin and G. E. Moore, 1958[6]). The two projects mentioned by these authors are one on pulmonary carcinoma with nitrogen mustard as the chemical adjuvant, and one on gastric carcinoma with thiotepa as adjuvant. In the second case, the first dose of thiotepa is injected into a portal vein at the completion of the operation.

[4] *Nature*, 1958, 182:1505 (November 29).
[5] *Brit. med. J.*, 1959, 1:1315 (May 23).
[6] *J. Amer. med. Ass.*, 1958, 167:1710 (August 2).

Current Comment.

HYPOCHONDRIASIS.

A RECONSIDERATION of our concepts regarding disease is a salutary exercise, and this has been done in the present issue by Phillip Greenberg in respect of hypochondriasis (see page 673). The term usually conjures up the picture of a man of middle age, who complains wearisomely of abdominal pains and discomforts for which no physical basis has been revealed. In the days when the syndrome was given the dignity of a special section in textbooks, it was referred to across the English Channel as "the English malady". As Greenberg reminds us, hypochondriasis was regarded as the male counterpart of hysteria in women; and, as with hysteria, the diagnosis came to be attached to symptoms not limited to abdominal and pelvic organs. In their concept of hypochondriasis as a symptom rather than as a well defined syndrome, Macalpine and Hunter, whom Greenberg quotes, adopt the psychosomatic approach and urge psychiatrists to pay more attention to physical symptoms in their patients. One might add here that it is even more important for the general physician to determine the setting in which he meets symptoms which lack an organic pathological basis. Macalpine and Hunter regard hypochondriasis in particular and psychosomatic symptoms in general as expressions of "the primitive body-mind unit", with different degrees of divorce from reality, ranging between simple morbid preoccupation and delusional states. Nearly seventy years ago Sir George Savage[1] suggested that hypochrondriasis might be regarded as being due either to imperfect evolution, in which case bodily functions which should become automatic continue to make their impact on consciousness, or to mental dissolution, as in the case of the elderly hypochondriac, when these functions again become consciously performed after having been performed unconsciously for many years. Certainly patients with prominent hypochondriacal symptoms are unhappy people, insecure, lacking in self-confidence and tending to evade responsibility. As Kipling wrote:

> He that is costive of soul towards his fellow,
> Through the ways and the works and the woes of this life,
> Him food shall not fatten, him drink shall not mellow,
> And his innards shall brew him perpetual strife.

The hypochondriacal patient is notoriously resistant to efforts to change his basic attitude. Hence Freud rejected him from his category of true psychoneurosis. His suggestion of an organ pathology may some day be supported by demonstration of a biochemical basis for morbid cœnæsthesia. But while the hypochondriac is unresponsive to deep insight therapy, he may yet, as Greenberg points out, derive some benefit from, and even be checked from a further retreat from normality by, psychotherapy on more superficial levels. We must constantly be on guard against damning a patient with a diagnosis.

[1] Hack Tuke's "Dictionary of Psychological Medicine", London, 1892.

GENETICS, RADIOBIOLOGY AND RADIOLOGY.

THE proceedings have been published of a one-day meeting under the auspices of the Committee on Radiobiology of the Academy Research Council of the United States.[2] The purpose of the conference was to consider the hazards of radiation to the population and particularly the genetic effects of radiation, and to consider precautionary measures applicable to radiological practice. Some of the papers may be briefly summarized.

G. H. Mickey reviews concisely the mechanisms of radiation damage in living tissue, in an excellent chapter.

I. H. Herskowitz considers the concept of a "cluster" of ionizations being required to produce a given radiation effect. Radiation which produces large clusters by dense ionization is wasteful in regard to radiation effect produced in proportion to total energy absorbed. The presence of extra chromosomes (polypoidy) in cells increases the likelihood of radiation damage. Similarly, chromosomes tightly packed as in a sperm head are more liable to damage than those loosely arranged in a resting nucleus. In discussion of the oxygen effect, the author states that the number of chromosome breaks in cells irradiated with the same dose is proportional to the oxygen tension. But

[2] "Genetics, Radiobiology and Radiology Proceedings, Mid-Western Conference", by Wendell G. Scott, M.D., and Titus Evans, Ph.D.; 1959. Oxford: Blackwell Scientific Publications. 9" × 6", pp. 166, with 10 illustrations. Price: 42s. (English).

the presence of high oxygen tensions, while causing more breaks, also assists in the repair of broken chromosomes. Thus the cells which are subject to greater damage have greater capacity for repair of injury, and so much of the hoped-for benefit from raising oxygen tension in animals may not be realized in patients under radiation therapy.

J. F. Crow states that geneticists are becoming more anxious about human risks of radiation exposure since finding that the mutation rate in mice is 15 times greater than in Drosophila, dose for dose. Further, it is realized that recessive mutations are not completely recessive, and that it is not necessary to wait for the union of two recessives for some effect to be shown. In other words, some effects of radiation to recently exposed humans are likely to appear in generations immediately, not remotely, ahead. These may be minor impairments which make the individual less able to cope with ordinary life and so shorten the life span.

A. M. Brues discusses the relationships between leukæmia and radiation exposure. He argues that the situation is more complex than can be explained by a single-point mutation effect as inferred by Court, Brown and Doll. He criticizes the statistics of these authors, who deduced from them a linear relationship indicating a single-hit response effect. Brues has reviewed the Japanese Leukæmia cases, and states that on present evidence only doses above 100 *r* have been leukæmogenic. He quotes the work of Lewis, who established a threshold for the leukæmic hazard at the 70 *r* level. There certainly is no straight-line relationship between dose and appearance of lymphatic tumours in mice. But our perspective must be maintained; a leukæmic child has a greater probability by a factor of 2 that he was radiologically examined in utero. In Farber's clinic an exactly similar probability exists for those leukæmic children whose mothers had been receiving antihistamine drugs during pregnancy.

A contribution by D. Gould gives advice on the reduction of radiation hazards during dental radiographic procedures. *Inter alia*, he advises the use of high kilovoltage and low milliamperage techniques with adequate beam filtration, together with faster screens, films and chemicals.

J. A. Campbell discusses similar problems in obstetrical radiology, and his contribution should be read by interested radiologists. He advises avoidance of any routine of radiological procedures, no radiological examination during early pregnancy, and adequate consultations between radiologist and obstetrician to minimize the number of films exposed. Among technical proceedings advocated are beam collimation, long target-film distances and the use of high kilovoltage, low milliamperage techniques, with well-filtered beam. Newly-developed ultra-fast screens, films and developing chemicals reduce exposure, while wedge filters placed over parts of uneven thickness produce more even films when used with lower ratio grids. A single erect lateral view provides maximum information with minimal exposure. A postero-anterior view with compression reduces corresponding antero-posterior thicknesses by about 10 cm. Central shielding allows pelvic mensuration, and reduces fœtal and maternal gonadal doses to one-tenth and one-third respectively. In cephalic presentations, maternal and fœtal gonads are situated well above the crests of the ilia, and screening above this level protects gonads during pelvimetry.

Verbatim reports of the discussions after each paper are given. The elimination from the reports of much unnecessary verbiage by the stricter use of the editorial blue pencil would have improved this volume. It has been well produced by Blackwell Scientific Publications.

HYPNOTISM.

WITHIN recent years there has been one of the recurrent renewals of interest in hypnotism as a form of therapy or as an adjunct to it. As with other methods, it should be conducted or controlled by medical men if the best results are to be obtained and patients are to be saved from danger and abuse. Hypnotism unfortunately has been exploited by charlatans and stage performers; this fact is partly the result and partly the cause of its neglect by the profession as a whole. In the last hundred years or so many books and papers on the use of hypnotism in medicine have appeared. But just as sucessive generations of surgeons forgot the lessons learned by their predecessors, for example, on the treatment of war wounds, so successive generations of doctors have forgotten the lessons learned over the years about hypnotism in therapy.

Hitherto, most of the papers on hypnotism have appeared in journals catering mainly for the general practitioner and physician, but recently two purely surgical journals have published articles on its use in surgery. The first of the articles is entitled "Hypnosis as an Adjunct to Surgical Therapy" and is by a group of physicians, headed by R. C. Doberneck, and the well known surgeon Owen Wangensteen, who visited Australia recently.[1] This records the treatment with hypnosis of 99 patients, who were divided into five groups. In the first group were 32 patients with the post-gastrectomy syndrome. Recurrent ulcer and other organic disease were excluded, gastric acidity and peptic activity were assessed, and inquiry was made about the effect of stress and diet on symptoms. The patients were then told to eat anything they wanted and even previously offending food. Under hypnotic suggestion 26 of the 32 gained weight and 30 had symptomatic improvement; 12 of the 32 not only gained weight but also became completely free of symptoms. In an earlier paper,[2] Wangensteen and others have emphasized the usual failure with drug, dietary and surgical treatment and the frequency of psychological abnormalities in these patients. They state that the response to this form of therapy (hypnotic suggestion) has been so much superior to that observed in this same group of patients given all other forms of therapy that they are persuaded that this inquiry warrants continued study.

The second group consisted of patients with post-operative pain. Pre-operative hypnosis was used for 31 patients awaiting operation for non-malignant abdominal conditions; there was also a control group of 31. Suggestions were given to the selected group against post-operative pain, the discomfort of tubes etc., and also suggestions that they should cooperate with the staff. They were told that they could have narcotic drugs if necessary. All the patients in the selected group said that they found the post-operative period less trying than was expected, and most of them retained a cheerful and helpful attitude; they used far fewer narcotic drugs than the control group. "Bizarre forms of pain" characterized the third group, which consisted of 17 patients. The best results were obtained with those who had the phantom limb syndrome and those in pain from metastatic cancer. Two patients were relieved of pain after cordotomy had failed to give relief. In the fourth group, which consisted of 11 patients with obesity, the aim was to reduce weight without producing the usual discomfort of dietary restriction. They were given a reducing diet reinforced with suitable hypnotic suggestions. There were six failures in this group; the remaining five not only lost weight but succeeded in keeping it at the reduced level. In all of them various dietary measures alone had failed. Hypnoanæsthesia was used in the fifth group. Encouraging results were obtained with endoscopic examinations and minor surgical operations. Some success followed preliminary suggestions against post-operative pain as noted above, and tests are being made of hypnosis during the induction of general anæsthesia for major operations.

The second article is by Herbert A. Ecker,[3] who describes the benefits of hypnosis for a girl who suffered serious facial injuries. It shows how useful hypnosis can be with patients for whom general anæsthesia would be particularly difficult or dangerous.

[1] *Surgery*, 1959, 46: 299 (August).
[2] *J. Amer. med. Ass.*, 1957, 165: 1957 (December 14).
[3] *Amer. J. Surg.*, December, 1959.

Abstracts from Medical Literature.

RADIOLOGY.

Reiter's Disease, Rheumatoid Arthritis and Ankylosing Spondylitis.

R. M. MASON *et alii* (*J. Bone Jt Surg.*, February, 1959) discuss the differential radiological diagnosis of Reiter's disease, rheumatoid arthritis and ankylosing spondylitis. In Reiter's disease the changes are predominantly in the feet and sacro-iliac joints. In the feet, in addition to destructive joint changes and consequent deformity, exuberant (as opposed to simple linear) periosteal new bone formation tends to occur on the calcaneum, and it may also occur to a less extent at the wrist. Asymmetrical bone and joint involvement is a characteristic but not invariable feature, whereas generalized osteoporosis is not. Hand changes are mild, even when the wrist is severely involved. The authors consider that the presence of large rough spurs with fluffy periosteal new bone on the plantar surface of the calcaneum is characteristic of Reiter's disease. In rheumatoid arthritis there is a tendency for changes to be symmetrical, to be associated with osteoporosis and to affect hands and feet equally. The sacro-iliac joints, when affected, show only mild changes. In most patients with ankylosing spondylitis the great predominance and early appearance of sacro-iliac changes and the mild involvement of the feet are in contrast to the severe affection of the feet and late development of sacro-iliitis in Reiter's disease.

Functional Disturbances of the Gastro-Intestinal Tract.

T. E. MACHELLA (*Radiology*, September 1959) states that patients with symptoms attributable to functional motor disturbances of the gastro-intestinal tract are frequently encountered. Often they are subjected to a variety of laboratory and radiological examinations, but, because no evidence of organic disease is found, are offered no satisfactory explanation for their symptoms other than that these are due to "nerves". In the majority of such instances, the correct diagnosis may be made by an evaluation of the presenting symptoms in terms of physiological changes and an elucidation of the underlying emotional disorder suggested by their presence. The radiologist may be of invaluable assistance in the diagnosis by calling attention to and reporting all motor disturbances encountered during his examinations. Motor abnormalities occur in patients subjected to frustrating, stressful life situations. In general—though not invariably—anger, resentment and hostility cause motor disturbances similar to those which follow excitation of the parasympathetic division of the autonomic nervous system, while fear and sadness mimic the actions of the sympathetic system. The functional disturbances which appear to be due to predominantly parasympathetic influences are œsophagospasm, gastric hypermotility, duodenal spasm and hypermotility, and spastic disorders of the small and large intestine. Those which appear to be due to sympathetic hyperactivity or parasympathetic underactivity include achalasia of the œsophagus, gastric retention in the absence of obstruction, megaduodenum, and hypoactive states of the colon, including "psychogenic" megacolon. Management consists of an attempt to help the patient solve his emotional problems, as well as the administration of drugs to correct the abnormal physiological state. Somatic changes may occur when functional disturbances persist. For example, achalasia of the cardia may lead to megaœsophagus, and high intraluminal pressures in the irritable colon to diverticulosis and its various complications. It must be emphasized that before symptoms are ascribed to functional motor disturbances, the possibility of organic disease should always be carefully ruled out.

X-Ray Diagnosis of Bile Duct Calculi.

E. SALZMAN, R. P. SPURK AND D. H. WATKINS (*Gastroenterology*, November, 1959) review the non-operative X-ray diagnostic procedures which identify stones in the bile ducts. In the past seven years several important advances have been achieved in the non-surgical X-ray diagnosis of bile duct calculi by the use of contrast media. Oral cholangiography is most useful in patients who are sensitive to "Biligrafin". Intravenous cholangiography is the best method available for visualization of the bile ducts, but usually fails in the presence of jaundice. Biliary calculography is a procedure to identify opaque gall-stones by prolonged oral administration of a cholecystographic contrast medium. The vast majority of bile-duct calculi may apparently be identified by this method, although a larger experience is required for accurate evaluation. Biliary calculography is probably the most useful procedure to demonstrate bile duct calculi in the presence of jaundice and to show calculi within the intrahepatic ducts. A substantial incidence of failure, however, is inherent in all of these tests. Each of these procedures may be employed successfully after one of the other methods has failed. All methods fail to visualize the ducts or identify bile duct calculi in the patient with a high degree of bile duct obstruction or liver insufficiency.

Lumbo-Sacral Inter-Body Spinal Fusion.

G. F. DOMMISSE (*J. Bone Jt Surg.*, February, 1959) discusses the results of lumbo-sacral inter-body spinal fusion in a series of 48 patients. He states that the success of spinal fusion is best shown radiologically in antero-posterior views and in lateral views in flexion and extension. Absorption of the grafts and replacement by visible new bone, the absence of encapsulation or sequestration of the grafts, and failure to demonstrate mobility on flexion and extension of the spine are the most important radiological features, all of which must be present before a successful fusion may be claimed. Failure of spinal fusion is much more easily recognized, and in some of the patients under review there has been complete absorption of the grafts. In others the grafts have become encapsulated and have remained unchanged, without any lessening of spinal instability. In yet other patients a pseudarthrosis has developed, which is easily recognized radiologically.

Bone Changes in Adult Cretins.

I. B. D. MIDDLEMASS (*Brit. J. Radiol.*, October, 1959) discusses the bone changes sometimes found in adult cretins. The changes—with the exception of enlargement of the pituitary fossa, which occurs in some cases—are the obvious end-results of abnormalities which are more familiar in infancy and childhood. These include retarded skeletal development, epiphyseal dysgenesis and changes localized to the vertebral bodies at the dorso-lumbar junction. No "lines of arrested growth" were seen in the lumbar vertebræ, iliac bones or wrists of any of the adults. All those with large pituitary fossæ showed multiple abnormalities. These radiological appearances are of no practical value in diagnosis since this is painfully obvious on clinical grounds alone. However, they are of interest in showing the effects on the skeleton and pituitary gland of prolonged deprivation of thyroid hormone.

Staphylococcal Pneumonia in Children and Adults.

H. I. MEYERS AND G. JACOBSON (*Radiology*, May, 1959) state that the radiological findings in staphylococcal pneumonia serve to distinguish it from other types of pneumonia, especially in infants and small children. In adults the distinctive features seen in childhood are less commonly found and the ætiological diagnosis is usually not very evident radiologically. One of the most striking characteristics of the disease is the rapid change in the X-ray findings. The picture may change from one of minimal to one of very extensive involvement in a matter of hours. There is often little correlation between the radiological appearance and the clinical condition of the patient. The feature of least value in differentiating staphylococcal pneumonia from other types of the disease is the extent of pneumonic infiltration. This may be lobar or segmental in distribution, rarely bilateral, and has no distinguishing characteristics; in many cases it may be entirely obscured by other changes. Pleural effusion and empyema are very common, and their presence in a young infant is nearly pathognomonic. Effusion may not be demonstrable on the initial examination, but is usually present subsequently and may develop very rapidly. Not infrequently, empyema is seen in the first chest skiagram, and may be so extensive as to obscure everything else on the same side. Pneumatocele formation is a regular feature in staphylococcal pneumonia and is quite diagnostic. Pneumatoceles are thin-walled cyst-like areas which may or may not contain air-fluid levels. They tend to appear late in the course of the disease, but when seen early they are pathognomonic. They are differentiated from lung abscesses by their thin walls and their tendency to rapid change in appearance, size and

location. There is little correlation between the presence and number of pneumatoceles and the clinical condition. Pneumatoceles may disappear after brief periods or they may persist for several months. Eventually they disappear completely. Another characteristic finding in staphylococcal pneumonia is pneumothorax, usually a pyopneumothorax. This varies in extent from small, sometimes loculated areas, which may be hard to distinguish from pneumatoceles, to massive tension pneumothorax. Those infants and children that recover usually have no parenchymal findings after about three months, although pleural thickening may persist for some time.

PATHOLOGY.

Experimental Ulcerative Colitis.

J. B. KIRSNER *et alii* (*A.M.A. Arch. Path.*, October, 1959) have used the Auer principle to produce ulcerative colitis in rabbits. The Auer procedure is to sensitize an animal to an antigen and then localize the sensitivity reaction to some selected site by causing non-specific inflammation in that site. In this paper, the authors sensitized rabbits to egg albumen. Then, before challenging with the antigen, they caused irritation of the rectum and lower part of the colon by instillations of formalin solution. This was followed by congestion and œdema of the submucosa and mucosa with superficial ulceration. The lesions could not be elicited by the antigen-antibody reaction alone or by formalin alone. The irritation by the formalin is thought to cause localization of antigen and antibody in the bowel wall by increasing permeability in that site.

Prevention of Urinary Calculi in Rats.

W. B. GILL, B. FINLAYSON AND C. W. VERMEULEN (*J. Urol.* (*Baltimore*), August, 1959) have conducted experiments on rats to see if the addition of calcium to the diet (in the form of calcium lactate) has any effect on the formation of foreign-body stones in the bladder. Such phosphatic stones are formed on small zinc disks, which are weighed before and after a stone-growth period of six weeks. It was found that a high calcium diet prevented stone formation, although the exact mechanism in the urine could not be determined. There was a great rise in calcium excretion, and the urine became alkaline, both of which factors would favour stone formation. However, there was a fall in phosphorus excretion, and an increase in citrate output, and both of these factors would help to impede or prevent the formation of phosphatic stones. The authors thought that the disturbance of acid-base relations caused by the extra calcium might be introducing a confusing element. A second series of experiments was therefore conducted in which sodium bicarbonate was added as well as calcium. The urine became very alkaline and there was a marked elevation of urinary citrate concentration. In this case stone formation was not prevented. In a third set of experiments, ammonium chloride (an acidifier) was added to the high calcium diet. The effect of calcium lactate in alkalizing the urine was prevented in varying degrees, and stone formation did not occur in this group. The authors therefore conclude that the stone-inhibiting action of the high calcium diet is not dependent on the accompanying disturbances in acid-base relations, and consider that the added calcium prevents stone formation because of the extreme reduction in urinary phosphorus levels. This occurs because a highly insoluble calcium phosphate is formed in the bowel. The authors suggest that there is a critical level of urinary phosphorus below which stone formation no longer occurs, even if the concentration of calcium rises very much, as with this diet. To judge by these experiments, the dietary ratio of calcium to phosphate is therefore of great importance in stone formation. The authors refer to a previous paper in which they demonstrated a converse shift by feeding rats with excess phosphate. This caused a high phosphorus level in the urine but a heavy fall in calcium, with consequent production of phosphatic stones both of the magnesium and calcium types.

Sclerosing Retroperitonitis and Sclerosing Mediastinitis.

W. A. HAWK AND J. B. HAZARD (*Amer. J. clin. Path.*, October, 1959) have reviewed the literature of sclerosing retroperitonitis and sclerosing mediastinitis and have added six examples of their own, five of sclerosing retroperitonitis and one of sclerosing mediastinitis. In both disorders the onset is insidious, occurring over a period which varies from days to years, but which is usually about three months. In sclerosing retroperitonitis the symptoms are mainly related to obstruction of the urinary tract, whereas obstruction of the superior vena cava usually results from sclerosing mediastinitis. In the latter condition œsophageal or aortic obstruction may occur and obstruction of pulmonary veins has been described. The pathological features are cicatrization with a variable amount of inflammatory infiltration. The appearance is not unlike that of Riedel's struma. The pathogenesis is not known as symptoms occur only when dense fibrosis has been well established. Diagnosis usually requires thoracotomy or laparotomy. Corticosteroids have given some success.

Hyperparathyroidism.

G. KLEINFELD (*Cancer*, September-October, 1959) has analysed the data concerning 63 functioning adenomata of the parathyroid gland encountered in the Presbyterian Hospital, New York, between 1906 and 1957. Two were recurrent adenomata, making a total of 61 adenomata in 59 patients. Two other tumours were functioning parathyroid carcinomata and are presented separately. There was no correlation between the histopathological findings and the clinical syndrome, although there was a relationship between the pre-operative serum calcium levels and tumour size, the adenomata being larger as the serum calcium level rose. Furthermore, larger tumours were found in those patients with skeletal involvement than in those without skeletal disease. The smallest tumours were in patients with calcium levels of less than 14 mg. per 100 ml. and in those with renal involvement only. In these cases the tumour was usually about 1 cm. in its greatest dimension. Because most of the tumours are in the neck, the author recommends that in case of failure to find a tumour, the surgeon should not go ahead with sternum-splitting operations. Because of the occasional diagnostic pitfalls of rapid frozen section examination, the surgeon should wait until all the removed tissue has been examined more leisurely by paraffin sections. The author stresses that the surgeon should incise the thyroid and carry out partial thyroidectomy in the search for embedded parathyroid adenomata. He also recommends diagnostic exploration of the neck when the clinical data are equivocal.

Fœtal and Post-Natal Atelectasis.

J. TANNENBERG (*Amer. J. clin. Path.*, October, 1959) has studied the lungs from fœtuses, stillborn babies and babies that died in the neonatal period. He states that in the broncho-alveolar spaces during fœtal life there is fluid which is free from cells and histologically demonstrable protein. This is physiological fœtal atelectasis. In the pathological fœtal atelectasis seen in stillborn infants, squames and albuminous fluid are present, owing to efforts at respiration resulting from temporary or intermittent anoxia, which may be caused by stretching or twisting of the umbilical cord. With respiratory movements after birth the fluid in the broncho-alveolar space is rapidly absorbed. Post-natal atelectasis the author regards as being comparable to that produced in animal experiments by bronchial obstruction, and post-natal atelectasis accompanied by exudative processes is thought to be due to circulatory disturbances. The author suggests that hyaline membranes in the lung are a complication of post-natal atelectasis and merely an index of cardiac decompensation rather than a primary condition.

Autoantibodies in Human Ulcerative Colitis.

O. BROBERGER AND P. PERLMAN (*J. exp. Med.*, November, 1959) have examined the sera from 30 children suffering from ulcerative colitis. They demonstrated a precipitating and hæmagglutinating factor in most sera, which reacted with a constituent of human colonic tissue obtained from newborn children shortly after death. The factor could also be prepared from fœtal tissue. Serum from certain patients reacted also with extracts of liver and kidney. Sera from healthy controls did not give any reaction, although a few sera from children with nephrosis, acute nephritis and rheumatoid arthritis contained precipitating and hæmagglutinating antibodies against extracts of colon, liver and kidney. The authors also discuss the possible mode of antibody formation and favour the hypothesis that antibody to an antigen derived from an invading organism may have a cross reaction with a similar antigen in the host's tissues.

Brush Up Your Medicine.

THE TREATMENT OF CHRONIC BRONCHITIS AND BRONCHIECTASIS.

Terminology.

For clinical purposes, chronic bronchitis may be defined as a condition characterized by persistent cough and sputum for which no other cause is found. This definition is unambiguous, although it includes mild or early cases in which probably no treatment is required. Undue dyspnœa on exertion is sometimes given as one of the criteria; but this is not always present even in cases warranting treatment, and its presence implies the presence of either bronchospasm or emphysema as well. "Catarrhal bronchitis", exemplified by most cases of "smoker's cough", is present when the sputum is mucoid; the term "infective bronchitis" is applied to cases in which the sputum is purulent or mucopurulent. Infective exacerbations of chronic catarrhal bronchitis are common, especially in winter; exacerbations of infective bronchitis characterized by an increase in the quantity and/or purulence of the sputum are similarly common. "Asthmatic bronchitis" is a descriptive term indicating that wheezing is a prominent feature. In view of the impossibility of producing a generally acceptable definition of asthma, the non-committal term "wheezing bronchitis" is preferred, particularly as a minor degree of wheeze is demonstrable, clinically or by appropriate functional tests, in almost all patients with chronic bronchitis at some time. "Allergic bronchitis" is also incapable of precise definition, and the term could well be discarded. However, the presence of an allergic element in bronchitic patients may be suspected from the history, the presence of œdematous nasal mucosa and eosinophilia in sputum or blood.

The dual label of "chronic bronchitis and emphysema" is frequently loosely used. However justifiable this may be histologically—and bronchitis frequently, if not always, implies bronchiolitis with its sequelæ—it is not justifiable clinically unless there is permanent reduction in exercise tolerance in relation to age. This applies irrespective of the alleged physical signs in the chest. The distinction is clinically important, because the prognosis is worse for subjects with reduced exercise tolerance, and intensive treatment is therefore all the more important in this group.

Bronchiectasis means dilated bronchi. The diagnosis ultimately rests on bronchography, although the condition may be suspected from the history, physical examination and chest radiograph. The differentiation of the classical types of bronchiectasis (cylindrical or saccular, for example) is of less practical significance than the definition of the level of the bronchial tree affected and of the distribution of the abnormality. Classical bronchiectasis affects the large bronchi, the smaller bronchi and bronchioles being obliterated; typically this condition follows lobar or segmental collapse, and it may therefore be relatively localized. Dilatation of segmental and subsegmental bronchi, and also of bronchioles, often irregular and widespread, may occur in chronic bronchitis, but it is then part of a generalized process, even though the changes are usually less marked in the upper lobes. The clinical significance of the distinction lies in the fact that the localized condition is potentially suitable for surgery. There is thus some advantage in restricting the term "bronchiectasis" to the classical varieties affecting large bronchi, but it is at variance with the literal meaning to exclude any form of bronchial dilatation; it is also true that varieties intermediate between "true" bronchiectasis and bronchitis are sometimes seen. Diffuse bronchitic changes may also occur in association with localized "classical" bronchiectasis.

Investigations.

At some stage all patients with bronchitis or bronchiectasis require a chest radiograph to exclude other conditions; this applies particularly to the elderly "chronic bronchitic", who sometimes has open pulmonary tuberculosis of a low grade of activity, or who may develop a carcinoma with little change in symptoms. During or after exacerbations of bronchitis, further films may be necessary to exclude complications or associated conditions such as pneumonia, spontaneous pneumothorax or carcinoma. Both bronchitis and bronchiectasis may occur with apparently normal plain radiographs. Bronchography is required in a minority of cases, notably in those in which surgery may be indicated if a localized area of disease is demonstrable, and therefore chiefly for younger patients and for those whose exercise tolerance is not seriously reduced. X-ray films of the nasal sinuses are desirable for patients with nasal symptoms; these, with the history and physical findings, indicate whether further allergic or rhinological investigation is required.

The most useful routine investigation is microscopic examination of the sputum stained by Leishman's method. Mucoid sputum may be "cloudy", owing to the presence of epithelial cells and debris; a yellow or creamy colour of the sputum may be due to eosinophils or polymorphs, or a mixture of both. The results of microscopic examination of the sputum are sometimes surprising, and the implications are important. Patients with mucoid or eosinophilic sputum will not as a rule benefit from antibiotic therapy. Sputum eosinophilia suggests a search for an allergic factor; if (on other grounds) steroid therapy is indicated, it is in these cases that the best results are usually obtained. Polymorphs in the sputum indicate active infection with a pathogenic organism which appropriate antibiotic therapy will diminish and often remove.

Sputum cultures and antibiotic sensitivity tests are interesting and occasionally invaluable, but treatment can be effective and economical without them. Preliminary homogenization of the sputum is essential for reliable results, and the use of a selective medium for *Hæmophilus influenzæ* is desirable. In patients with persistently purulent sputum *H. influenzæ* is the commonest pathogen, although a single "routine" culture may fail to reveal it for various reasons; pneumococci may be found in addition. In patients who have occasional infective exacerbations, but whose sputum is usually mucoid, a pneumococcus alone is frequently found. Other pathogenic organisms isolated less frequently are Friedländer's bacillus, *Staphylococcus aureus* and a variant of *Bacterium coli*.

The simpler spirometric tests of ventilatory capacity (the vital capacity and volume of gas expired in the first second of forced expiration) are a good objective index of disability, and hence of progress and therapeutic response. If the tests are performed before and after a bronchodilator drug has been given, a good estimate of the proportion of structural as opposed to functional change may be made, an appreciation of which is a useful therapeutic guide and a valuable aid in prognosis. Ventilatory capacity tests are indicated notably for younger patients complaining of reduced exercise tolerance, and for those whose condition is deteriorating in spite of treatment. In doubtful cases of mould or house-dust sensitivity, inhalation tests using ventilatory capacity as an index are diagnostic.

As an objective assessment of functional disorder, these tests are also useful when compensation claims are likely to arise. They are also a wise precaution prior to surgical procedures, either thoracic or abdominal, on severely bronchitic patients with impaired exercise tolerance, so that the risks of post-operative complications may be more accurately assessed. The estimation of differential lung function is sometimes necessary before resection is undertaken; this requires fluoroscopy and bronchospirometry in addition to over-all tests.

Domestic and Occupational Measures.

Smoking should stop on diagnosis, but I know of no way by which this advice may easily be carried out. Some patients change from cigarettes to a pipe, with apparent benefit.

The following counsels of perfection must obviously be modified according to circumstances; probably the greater value of these suggestions lies not in their immediate adoption, but in their influence on plans and decisions affecting the future of the patient and his family. Ideally, the patient with chronic bronchitis should live in a temperate climate with few extremes or sudden changes of temperature. A rural rather than an industrial atmosphere is also preferable. The bedroom, living room and bathroom should all be heated prior to use in winter, and the bedroom in particular should at the same time be reasonably well ventilated. A relatively dust-free bedroom is obtained by reducing furniture and floor coverings to a minimum, by waxing floors and providing washable curtains, and by using a rubber mattress and pillow or plastic pillow and mattress cases; these measures are worth suggesting to all patients with nocturnal cough or wheeze.

School-children, as the source of most upper respiratory tract infections in a family, are a disadvantage in the home from this point of view; elderly bronchitic patients with any choice in the matter may prefer to keep their distance. The home should be close to the patient's work and close to transport. Extremes of environment, in terms

of heat, cold, dust, humidity or overcrowding, are undesirable at work. A change should be made to a sedentary job before disability is severe and work absences become frequent or prolonged. On the other hand, a change of job is not recommended lightly; a seemingly strenuous occupation in which the patient is skilled may be easier than one which appears lighter but is unfamiliar. Advice will clearly depend on many factors, including length of service with the present employer, educational standards and opportunities for retraining or for obtaining alternative work with the same employer; but in any case the aim is to keep the patient at remunerative work for as long as possible. Once out of a job, these patients are difficult to place again, and one often wishes that more opportunity for piece-work existed for them.

Physiotherapy.

Two physiotherapeutic techniques are of value: breathing exercises and postural drainage and/or postural coughing.

Breathing exercises are indicated when exercise tolerance is significantly reduced, when there is evidence of anxiety or of emotional overlay, and when wheezing and its associated pattern of upper thoracic breathing are present. The chief principle involved is the attainment of relaxation, both mental and physical. Success in this aim ensures the restoration of the normal pattern of "abdominal" and lower thoracic breathing; there is good evidence not only that this form of breathing is more economical in terms of muscular work, but also that it is correlated with relief of asthmatic symptoms. Contrary to common physiotherapeutic teaching, active forced or prolonged expiratory efforts are contraindicated; the stress should be placed on efficient inspiration. The exercises are mastered at rest, and later during exercise graduated according to the patient's exercise tolerance.

Postural drainage simply invokes the aid of gravity in clearing accumulated secretion. The foot of the bed is raised on blocks nine to 12 inches high, and the patient lies for several minutes in the prone, supine and right and left lateral positions. More precise positioning to drain specific bronchi is described, but is usually superfluous. Positions in which coughing produces no sputum may be deleted except during exacerbations.

In each of the positions adopted the patient coughs deliberately; the cough may be aided by manual percussion or compression of the chest. Sputum is often "shifted" by taking a deep inspiration and then expiring suddenly, forcibly and completely. Paroxysms of coughing, a rapid succession of coughs without intervening inspiration, must be controlled by the patient; each cough should be preceded by a breath in. Coughs in the end-expiratory position are as distressing as they are ineffective.

A full regimen of postural drainage may take half an hour to one hour. This is practicable in hospital, but patients will not usually spare so much time once or twice a day at home. Patients are therefore taught to control the duration of each position by the volume of sputum produced; most of the removable sputum is produced within two or three minutes of positioning and coughing, although children may require rather longer. When the volume of sputum produced falls, the posturing is reduced to once daily, and the duration may also be reduced. Duration and frequency are increased at the onset of a head cold or an increase in the volume and/or purulence of the sputum. It is found that the shortened routine soon becomes part of the patient's morning ritual, and is not a bugbear to be avoided on any slight excuse. Some patients, particularly those with respiratory embarrassment, cannot be postured for more than a few seconds at a time, but often the period can be gradually increased.

The use of antibiotics is an adjunct to physiotherapy and not an alternative, particularly in bronchiectasis; the effectiveness of antibiotics is reduced if sputum is allowed to accumulate. A common sequence is physiotherapy plus antibiotics initially followed by a trial of physiotherapy alone; antibiotics are reintroduced intermittently for exacerbations, or continuously if sputum volume and purulence are not adequately controlled by physiotherapy alone.

Antibiotic Therapy.

Antibiotics will not benefit patients producing mucoid sputum or even mucopurulent sputum in amounts of less than one or two ounces per day. Acute exacerbations, characterized by increased quantity and purulence of the sputum, in patients in these groups should probably be treated with antibiotics, particularly when the attacks are known to last for long periods if untreated, or when the bronchitis is already associated with diminished exercise tolerance and it is desired to minimize further lung damage.

If the exacerbations are infrequent—less than three or four a year—infection with a pneumococcus may be responsible, so that "Penicillin V" given orally in a dosage of 500 mg. four or five times a day may be effective. A change is made to tetracycline if no response in the quality of the sputum is apparent in 48 hours.

Patients with chronically purulent sputum may be given a trial of oral penicillin therapy, but in my experience it is rarely successful; the causative organism in these circumstances is usually *H. influenzæ*, which is commonly relatively insensitive to penicillin. Reduction in the quantity and purulence of sputum is usually achieved within three days with tetracycline in a dosage of 750 mg. every six hours; after two or three days the dose is reduced by 1 gramme every two or three days until 1 gramme daily is taken. It is stresed that the usual dose of 1 gramme per day is inadequate to effect initial control of severe bronchial infection, although this dose may be adequate subsequently to maintain the sputum relatively free of pus. For patients in hospital, in whom tuberculosis has been excluded and renal function shown to be adequate, and who are not aged or grossly arteriosclerotic, the combination of penicillin, 4,000,000 units per day, and streptomycin 1 to 2 grammes per day in two to four divided doses, gives effective initial control. Chloramphenicol is also extremely efficient; but as these patients may need repeated or prolonged courses, its use cannot be recommended as a routine measure.

The total duration of a course of antibiotic therapy in "acute on chronic" bronchitis will depend upon the severity and on the response. Once it is decided that antibiotics are necessary, the course should rarely last less than a week, and it should usually be continued for 10 to 14 days. If purulence of the sputum returns within two or three weeks of the cessation of treatment, it is likely that *H. influenzæ* infection is present; ideally bacteriological confirmation should be sought at this stage. Again, the decision to use antibiotics in the first place having been made, there is no logical alternative but to begin treatment again unless the degree of purulence is slight. Similar initial doses are required, and the course should probably be continued for six to eight weeks or until the advent of warm weather.

Patients with severe chronic bronchitis or bronchiectasis producing more than three or four ounces of highly purulent sputum per day should almost certainly have either long-term continuous or intermittent chemotherapy. Which of these alternatives should be adopted is a matter of opinion and debate; both have their merits and demerits. Probably, in the present state of knowledge, the decision is best made on the progress of the individual patient. Patients should at least be given one chance during the summer months of giving up their antibiotic; some patients with bronchitis and bronchiectasis can be managed with winter courses only. Long-term therapy is almost invariably carried out with tetracycline, commencing in the doses given above. The maintenance dosage, which is controlled by the degree of purulence of the sputum, varies between 0·5 and 1·5 grammes per day. Patients are instructed to increase this dosage to 2 or 3 grammes per day when they feel a cold developing, or when the colour of the sputum tends to become more yellow; increased dosage is continued for two or three days and then gradually reduced. Rapid recurrence of purulence when the maintenance dose is reached indicates that the latter dosage is too low. Long-term oral penicillin therapy is valueless (pneumococci do not tend to recur rapidly if treatment is stopped, while *H. influenzæ* is not inhibited), and the use of chloramphenicol in this way is contraindicated. The newer long-acting sulphonamides are said to have a place in the management of recurrent bronchitis in children; they have no place in the treatment of adults.

The complications of continuous therapy with tetracycline are few. Tolerance of minor alterations of bowel habit is usually rapidly acquired, and the more severe disturbances are infrequent in spite of the higher dosage. Troublesome gastro-intestinal side effects are more frequent in out-patients than in in-patients, probably because the very slight risk of severe enteritis necessitates the issue of some warnings to the former. Side effects, as well as monilial infections, are possibly even less frequent with the new proprietary preparations containing both tetracycline and nystatin. If nausea or bowel disturbance necessitates stopping treatment in the early stages, a further attempt may be made after two or three weeks' rest and is frequently successful. An alternative is to

effect initial control by means of chloramphenicol or penicillin and streptomycin, and then to introduce tetracycline in maintenance dosage. Sometimes oxytetracycline is tolerated when tetracycline is not.

One of the possible hazards of continuous therapy with tetracycline is that the patient may become a carrier of staphylococcal strains resistant to this drug; these organisms are potentially pathogenic to the patient and his associates. This means that patients on tetracycline should not be given erythromycin either at the same time or on ceasing to take tetracycline, unless there are very strong and specific indications for its use; otherwise strains resistant to both drugs may develop.

The intermittent regimen requires that the patient be given a supply of tetracycline, which he takes at the onset of a cold or whenever his sputum becomes yellow. The dosage is as given above, and the drug is continued for three to ten days depending on developments. If courses have to be repeated more or less monthly, it is clear that continuous long-term therapy should be given instead.

Antibiotic therapy, either continuous or in frequent short courses, is required for a minority of patients with chronic bronchitis; nor is it necessary for all patients with bronchiectasis. However, in appropriate cases there is a striking improvement in appetite, weight, well-being and, frequently, exercise tolerance. Patients failing to benefit are usually those producing relatively small amounts of mucopurulent rather than purulent sputum. The argument that progressive damage to the lung is reduced to a minimum is not strong enough in most cases to justify continued antibiotic treatment in the absence of concurrent clinical improvement.

From the economic point of view, it has been shown in England that the decrease in time lost from work more than offsets the cost of treatment.

General Measures.

Cough suppressants are contraindicated by day, but may be useful on retiring or during the night for patients without copious sputum. Bouts of coughing are sometimes associated with bronchospasm, particularly in children, and may respond to theophylline (as "Theodrox" or "Choledyl" by mouth, or an aminophylline suppository) given on retiring, to a linctus containing "Benadryl", or to ephedrine at the time of the attack; mild sedation with "Amytal" or phenobarbitone may be added.

On waking and on going to bed the lungs should be cleared of sputum as far as possible, if not by postural coughing, then by forced expiration and deliberate coughing. An inhalation of friar's balsam or menthol may assist. Half an ounce of a mixture containing 5 grains of sodium chloride, 10 grains of sodium bicarbonate and 3 minims of spirit of chloroform, sipped in a glass of hot water, is greatly valued by many patients; others find tea or coffee an adequate substitute.

The sputum in bronchitis and bronchiectasis is not usually tenacious, but sometimes in the first few days of antibiotic therapy patients find it so. In these patients, and especially in those prone to wheezing, potassium iodide in large doses (10 to 20 grains three or four times daily) is an effective expectorant. Nothing is gained by adding other drugs to this mixture. Bronchodilator drugs also help at this stage, but are best given separately, so that the dosage and times of administration can be adjusted to suit the individual patient. Bronchodilator therapy, which is indicated for patients with wheezing as a symptom or sign and for patients whose exercise tolerance varies from time to time, is described in a subsequent article dealing with the management of emphysema. Mucolytic agent are rarely required in bronchitis and bronchiectasis, and are possibly little superior to water vapour in any case; the old-fashioned steam kettle is helpful, especially to children.

Steroid therapy has no place in the management of chronic bronchitis, unless for the acute exacerbation of severe wheezing tantamount to status asthmaticus; the more dramatic benefit is likely to occur only in those patients with significant sputum eosinophilia (with or without polymorphs as well).

The general health should be maintained by regular exercise within the limits of tolerance and by specific attention to diet; many patients become anorexic, lose weight and are found to be inadequately nourished. Weight gain above average limits is avoided; weight reduction in obese patients is invariably associated with improved exercise tolerance and well-being. Regular dental attention is desirable.

Vaccines.

Although there is evidence that some patients are "hypersensitive" to *H. influenzæ* as judged by skin reactions, there is no evidence to justify the use of *H. influenzæ* vaccines in courses intended to "desensitize" or "immunize" these subjects. "Non-specific" vaccines, containing *H. influenzæ*, are sometimes used for patients with "infective" or "intrinsic" asthma, a close relative of chronic bronchitis, but again the results are unimpressive. There is, however, scope for further investigation of vaccine therapy and for further controlled field trials. It may be mentioned here that desensitization to house dust is also disappointing, although a number of bronchitic patients show mildly positive skin reactions; it is worth a trial only for those who can clearly relate exposure to exacerbation of wheeze or nasal symptoms.

Although the relationship of viral infections to exacerbations of chronic bronchitis is not fully elucidated, epidemic influenza may certainly lead to aggravation of bronchitic symptoms, to bronchopneumonia or to staphylococcal or pneumococcal pneumonia. Prophylactic immunization is therefore reasonable when an epidemic is predicted and an appropriate vaccine is available; but "routine" periodic inoculation is probably not justified. Further work on this problem is also indicated.

Surgery.

Surgery is contraindicated for patients with generalized chronic bronchitis, even if it is associated with patchy bronchial dilatation. Bronchiectasis of the classical types, localized to one lobe or part therof and without bronchographic evidence of bronchitic changes elsewhere, is eminently suitable for resection of the affected area. However, the symptoms can usually be effectively controlled medically if the patient is prepared to accept a lifetime of postural drainage and possibly antibiotics. After adequate explanation, and perhaps after experience of the medical routine, the patient may reasonably be given the choice. Obviously, patients unlikely to submit to the tedium of medical management or unlikely to cooperate fully are better advised to have a resection at the outset. In general, patients with localized areas of bronchiectasis in both lungs are better managed by medical rather than surgical means. Bronchiectasis localized to one or two segments of one upper lobe, presumably post-tuberculous, is occasionally found on investigating hæmoptysis; surgery, or indeed active medical treatment, is rarely necessary in this group.

There is a group of patients in whom localized bronchiectasis is associated with some bronchitic changes elsewhere. Again as a general rule, to which there may be exceptions, these patients are better treated without resection, certainly if resection of more than one lobe seems to be indicated. The risks are that the patient's symptoms will be little relieved and that the bronchitis will progress; in either event, continuous medical treatment has not been avoided by surgery. Additional factors influencing one against surgery in this group are persistent chronic sinus infection and a strong family history of broncho-sinusitis. Persistent localized physical signs and the production of sputum almost exclusively in one specific posture during a period of medical management are prerequisites to considering resection in this group.

Pre-operative management includes attention to teeth, sinuses and infection, together with physiotherapy. Patients with any tendency to wheeze must have bronchodilator drugs throughout the pre-operative and post-operative phases, irrespective of the clinical signs; indeed, there is evidence that their routine use reduces the risk of post-operative pulmonary complications. A suitable routine is to give choline theophyllinate ("Choledyl") in a dosage of 200 mg. every six hours up to the day of operation, followed by an aminophylline suppository an hour before operation and thereafter every six to eight hours until "Choledyl" can be given again by mouth. Should wheezing or sputum retention occur in spite of this regimen, adrenaline by the subcutaneous route or an aerosol of adrenaline and ephedrine is given as an aid to physical therapy and whatever more active measures may be indicated.

Melbourne. BRYAN GANDEVIA.

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Research.

THE APPLICATION OF COMPUTERS TO BIOLOGY AND MEDICINE.

A SEMINAR on "The Application of Computers to Biology and Medicine" was arranged by the Baker Medical Research Institute, in conjunction with the Society of Medical and Biological Electronics, and held at the Baker Institute, Alfred Hospital, Melbourne on November 26, 1959. The chairman was Professor R. D. Wright, Professor of Physiology at the University of Melbourne, and the discussions were led by Dr. F. Hirst, of the C.S.I.R.O. Computer Laboratory, Melbourne, Mr. R. Rose, head of the Department of Industrial Electronics of the Royal Melbourne Technical College Radio School, Dr. T. E. Lowe, Director of the Baker Medical Research Institute, and Mr. J. Thacker, economist with the Department of Trade.

DR. F. HIRST dealt with the subject of digital computers. He said that those machines, as distinct from analogue computers, calculated in whole numbers and were an extension of the familiar mechanical desk computer. From the point of view of the user, their most important property was the high speed at which they could handle large masses of figures. Their major use in biology and medicine was in the field of statistics, in which their large capacity was of particular value in autocorrelation studies—for example, in the clinical testing of new drugs. Digital computers would undoubtedly find a use in the study of the structure of biological molecules, in which it might be desirable to test a number of hypotheses against numerical data. A recent example of that application was the use of a digital computer to analyse X-ray diffraction data in determining the structure of vitamin B_{12}.

MR. R. ROSE discussed analogue computers. He said that those machines converted physical measurements to electrical quantities. For example, in an analogue circuit blood pressure might be expressed as an electromotive force, and blood flow as a current. Those electrical quantities might be added, subtracted, divided, integrated and differentiated by combinations of various circuit elements—resistances, capacitances and amplifiers. If extreme accuracy was not required analogue computers could be constructed at moderate cost. They might be used to simulate an actual biological system, and had the tremendous advantage that the experimenter could visualize the logic of the system under study and test his conclusions by trial and error—a procedure carried out by switching of the different components of the computer. Analogue computers had a further advantage, in that it was possible to insert a living organism into the system, observe the behaviour of the computer, and then, by a process of trial and error, replace the organism with an arrangement of computer elements which would bring the system back to the same behaviour as observed with the organism.

DR. T. E. LOWE introduced the topic of simulation of biological phenomena by models, and gave a description of a model which had been used in the Baker Medical Research Institute to simulate the control of the fluid volume of the human body. He said that data from clinical observations on patients with œdema indicated that the fluid in the body could be considered as a storage system of many compartments, into which went a continuous regulated flow of fluid, and from which a continuous regulated outflow occurred. The fluid concerned was a solution of many electrolytes in water. It appeared that the outflow from the system was regulated by a mechanism sensitive to changes in the volume of some portion of the stored fluid and also of its osmotic pressure. There were some indications that those features also influenced the inflow. In addition, the forces controlling the partition of fluid between compartments and the circulatory system, which provided the fluid-conducting mechanism between the various parts of the system, seemed of importance. An hydraulic model with a compartmented storage and controlled inflow and outflow and circulation had been built in two duplicated parts, one representing the solvent and the other the solutes. That enabled both volume and osmotic pressure measurements to be simulated and used to control the various flows. At various stages of the investigation of the control of body fluid that model had been successfully used to indicate the over-all behaviour of such a system and to provide leads for further clinical studies.

MR. J. THACKER considered the problem of communication. He said that at its most elementary level that meant that those engaged in research in medicine and biology and those working with computers should understand each other's languages. One difficulty in the way of applying electronic computing techniques to most complex quantitative problems in biology and medicine lay in the design of experiments to make the best use of the computer. The electronic computer imposed a discipline upon the experimenter—the discipline of planning his experiment well ahead so that a suitable computer programme could be designed to be as economical and as comprehensive as possible. That usually meant that the experimenter should discuss his project with the computing centre while it was in the planning stage, because often those discussions could lead to improvements in both the logic and the economy of the experiment. The worst possible thing was to present the computing centre with a finished mass of previously undiscussed data.

The speakers' remarks aroused a keen discussion amongst the audience of 50 persons. Discussion ranged from the relative merits of digital and analogue computers for handling non-statistical data to the possibility of constructing an analogue of various metabolic pathways for teaching purposes.

In closing the meeting Professor R. D. Wright, the chairman, said that most of those present would leave the seminar knowing a little more than they did when they came. The afternoon had been a most notable contribution towards eliminating the problem of communication raised by Mr. Thacker.

British Medical Association.

VICTORIAN BRANCH: PREVENTIVE MEDICINE SECTION.

A MEETING of the Preventive Medicine Section of the Victorian Branch of the British Medical Association will be held on May 12, 1960, at 4.30 p.m., at the Medical Society Hall, 426 Albert Street, East Melbourne. Dr. E. Cunningham Dax, Chairman of the Mental Hygiene Authority, will speak on "The Prevention of Suicides". All those interested are invited to attend.

ANNUAL MEETING, AUCKLAND.

THE annual meeting of the British Medical Association, in conjunction with the biennial conference of the New Zealand Branch, will be held at Auckland on February 4 to 10, 1961. The list of section secretaries for the scientific programme of the meeting has been received from the Honorary Joint Secretary. All section secretaries are

anxious to know whether there are any members in Australia who wish to submit papers, apart from those who have already been in contact with the Honorary Joint Secretary. Interested members are asked to communicate directly with the appropriate section secretary. The list of section secretaries etc., is as follows:

Medicine.—Dr. D. McR. Hanna, 1A Alfred Street, Auckland, C.1.

Surgery.—Mr. J. W. F. Macky, "Ormond", 94 Remuera Road, Auckland, S.E.2.

Obstetrics and Gynæcology.—Mr. I. B. Faris, 6 Cintra Flats, Whitaker Place, Auckland, C.1.

General Practice.—Dr. T. D. C. Childs, Great North Road, Henderson, Auckland.

Anæsthesia.— Dr. W. J. Watt, Department of Anæsthesia, Auckland Hospital, Auckland, C.3.

Dermatology.—Dr. P. B. Fox, 11 Mount Street, Auckland, C.1.

Neurology and Neurosurgery.—Mr. S. P. Wrightson, Neurosurgical Unit, Auckland Hospital, Auckland, C.3.

Pathology.—Dr. S. E. Williams, Pathology Department, Green Lane Hospital, Auckland, S.E.3.

Ophthalmology.—Dr. C. C. Ring, 1 Alfred Street, Auckland, C.1.

Orthopædics.—Mr. H. G. Smith, 28 Princes Street, Auckland, C.1.

Oto-Rhino-Laryngology.—Mr. C. B. Cornish, 13 Symonds Street, Auckland, C.1.

Pædiatrics.—Dr. Alice Bush, "Merivale", 18 Symonds Street, Auckland, C.1.

Physical Medicine (Rheumatology).—Dr. F. H. Swan, 42 Hamilton Road, Herne Bay, Auckland, W.1.

Psychiatry.—Dr. H. R. Bennett, Kingseat Hospital, Private Bag, Papakura, New Zealand.

Radiology.—Dr. A. F. Crick, 25 Princes Street, Auckland, C.1.

Chairman of Programme Committee.—Mr. W. I. Cawkwell, 41 Symonds Street, Auckland, C.1.

Joint Honorary Secretaries, Programme Committee.—Mr. A. F. Hunter and Dr. P. F. Bartley, P.O. Box 3532, Auckland, C.1.

Out of the Past.

MEDICINE IN THE GUTTER[1].

[From the *Australasian Medical Gazette*, April, 1901].

"Saltimbancoes, quaksalvers and charlatans deceive the vulgar".—SIR THOMAS BROWNE.

The prating mountebank has a place in all communities, savage and civilised, and the blatant announcement of all his wares has resounded from the gutter in all the centuries. His following has not been limited to the humbler classes, although these, owing to a lower level of education, have suffered most from his charlatanry. The "vulgar" whom the author of Religio Medici refers to in the above quotation, include all common, unequally cultivated minds of all grades of society: and as many a modern instance can show, by no means excludes the soi-disant cultured sections of the community.

It is little wonder that such a favourable environment has kept the quack genus in life from generation to generation, and that, allowing for natural ronations of physiognomy, we can trace the representatives of the family amongst us at present day. He has given up his wonted place at the street corner. His means are now the printing press and the penny post, and through these he showers his literary productions on doctor and layman alike. Last indignity of all he has even aped the office of the editorial chair, and the profession is now treated to a daily supply of periodicals under such captivating names as the "Uric Acid Monthly", "Gleanings", the "O.D. Quarterly" and so on ad infinitum. A very large proportion of this literature comes to us from our cousins over the Pacific. The Americans are a great people: we may even say, though not we fear in the Old Testament sense, a peculiar people. They can fly high like the lark, and low like the swallow before a shower. The present issue in which we feel called upon to protest against pamphleteering quackery, contains a review of an American work that would do honour to our country. Such are the lights and shades of American professional life.

It appears that the canker is widespread. The number of qualified men who contribute testimonial letters in favour of this or that proprietary medicine is astonishing. The spontaneous restiveness of their effusions is worthy of a "testifying" Salvation Army brother.

To put jesting aside—we would first warn any injudicious colleague on this side, that in even seeming to encourage such chicanery they are playing into the hands of money-grubbing commercial adventurers and secondly, appeal to the more enlightened sections of the profession in the United States, to endeavour to stem the current and rescue the noblest of professions from degradation to the meanest of trades.

[1] From the original in the Mitchell Library, Sydney.

Correspondence.

GENERAL PHARMACEUTICAL BENEFITS.

SIR: The amended Pharmaceutical Benefits Scheme has produced a spate of letters in the Journal. The majority of the letters suggest that the Federal Council of the B.M.A. are a "supine" and timorous collection of doctors instructed by "supine" Branches. Not one letter has analysed the possible reasons why a Government should impose restrictions on a profession. There appears to be a lack of diagnostic ability within a profession which prides itself on being able to diagnose other people's illnesses.

Is it not a reasonable statement that the basic reason for restrictions on prescribing stems from the behaviour of a minority of the profession in practising medicine? The Minister has stated that since the cost of "free" drugs had risen steeply to £21,000,000, there was no alternative. He had stated some years previously that when oral diuretics had been made free the cost in the first year was £1,000,000.

No one has yet asked the Minister how many doctors have been before Medical Services' Committees of Inquiry regarding the use of pharmaceutical benefits or how many doctors should have been questioned but were allowed to continue because the Department of Health is too lenient: and in any case, the more drugs that are used the bigger is the stick to wield. No attempt is being made to "whitewash" the Minister for being a party to this scheme. It can be agreed wholeheartedly that the "Scheme" is a step towards the complete restriction of the profession under nationalization. The actions of the Minister could be appraised critically as to whether he has the interests of the medical profession at heart or obedience to the Party line.

Without stretching the available evidence, it can be stated that a minority of the profession have created a situation, by their prescribing habits, which has allowed a profession to be "pushed around", without any prior consultation.

This could be an opportunity to remind the profession that more and more of the voters are being mesmerized by the superficial advantages of the Welfare State. Added to this is the strong inference that "Governments" are committed to the idea of the Welfare State and that the forces behind the idea are too strong for a profession to halt. Many members of the medical profession in Australia feel that the framework for nationalizing the profession has been modelled within the Commonwealth departments concerned.

It should be remembered that, in England, a Government took advantage of a socialistic theme that incomes should be levelled throughout the community and dangled the virtues of a superannuation scheme before the rank and file. To reduce the reasons for the change to a few statements can be criticized on the grounds of over-simplification, but medicine is based on assessing symptoms and coming to a reasonable diagnosis. The introduction of the *National Health Act* in Great Britain was facilitated by the simultaneous appearance of a shrewd Minister of Health and an ununited profession into which he could drive wedges.

Accepting the introduction of the "5s. scheme" as another step to nationalization, has the profession thought of means

of "stockpiling" ammunition to fight any future move? This is doubtful. It requires a critical self-analysis by all sections of the profession. There are signs of divisions within the medical profession. The recent circular issued by a Branch will be the means of gauging the interest of members in their future, but will it produce a means of releasing the medical profession from the bonds of restriction and the increasing interference with the practice of medicine?

Do the sporadic entrances of academic and scientific bodies into medical politics indicate a further lack of cohesion among members of the profession? We have been told that this is the "Golden Age of Medicine in Australia" and that those who comprise Governments cannot be unaware of the prosperity of all sections of the profession. The actions of the minority are seized upon by political persons, and others who stand to gain, to hasten the day when the profession will be "whipped into line". This minority have found that patients do not object to being brought back repeatedly for consultation because it costs a few shillings under the medical benefits scheme. The financial burden of "operations of choice" has been greatly reduced. This leads to a discussion as to whether the Federal Council was "supine" and allowed itself to be "walked over". What weapons were available to resist effectively this recent move by the Government? The proposals to resist appeared definitely ineffective when placed against the effects on the voters who had been promised "benefits" by the Treasurer.

Finally, it is suggested that the medical profession have had this 5s. scheme forced on them because they have ignored the trends in political thinking. This "existence in ivory castles" has occurred at a time of economic prosperity leading to a slackening of the mental disciplines necessary to preserve the traditions of good medicine and meet the changing needs of the community. The difference in thinking by various sections of the profession may be settled with the formation of an association in Australia. The Federal Council will fight provided they can present the community with the facts, based on a disciplined profession, which will show that the profession can provide at a reasonable cost and more efficiently a community service which needs no restrictions. Ways and means of disputing with the Government whether the "5s scheme" is in the best interests of the community will depend on the results in the next few months, and whether the profession will be united in any drastic action recommended.

Yours, etc.,

"SIC ITUR AD CANES".

SIR: Re letter by W. L. Calov in the Journal of April 2, 1960. W. L. Calov is a veritable "King Canute". He would have more chance with the tides than with politico-medical trends. He must by now realize that the B.M.A. is run by the few for the benefit of the few. The rank and file members are purely a source of finance, and ultimately the profession will be sold out to the Australian Government as surely as the British profession was years ago.

We could do something about it but we won't. As a whole we are thoroughly disorganized, with very little idea of what we want, and no time or inclination to do anything about it anyway. So, perhaps we deserve what we get.

Yours, etc.,

528 Albany Highway,
Victoria Park, W.A.
Undated.

DOUGLAS HILL.

"TOFRANIL."

SIR: Dr. A. Bartholomew in his letter (MED. J. AUST., April 2, 1960) concerning our preliminary report on imipramine (March 12, 1960) implies that our main study should be an adequately controlled one if it is to show how effective this drug may be. However, published reports such as those of Ball and Kiloh,[1] and Leyberg and Denmark,[2] seem to have answered the question "whether" this drug is useful or not affirmatively, leaving room for studies of the effects of "Tofranil" on individual patients whose histories are well known which might contribute something towards answering the question "how" effective it may be. This method is not unknown in evaluation of *the effects of leucotomy, and has usefulness in proportion* to the psychiatrist's knowledge of the patients selected.

The use of "Tofranil" is unlikely to prove a passing fad, and in view of the risk of suicide in patients with endogenous depression, it does seem unwise to add to that risk through delay in the case of those involved in a "double blind" study who would receive inert control tablets first in the course of random selection.

Yours, etc.,

6 Irilbarra Road,
Canterbury, E.7,
Victoria.
April 7, 1960.

R. E. G. MACLEAN.

SIR: It would be regrettable if Dr. Bartholomew's letter on "Tofranil" (MED. J. AUST., April 2, 1960) were to convey to the profession the idea that this is not a potent and useful drug in the treatment of depression. It is therefore advisable to examine some of the points he raises in objection to the findings of Stoller[1] and MacLean *et alii*[2] with regard to "Tofranil".

It is not always correct to say that drug evaluation trials are "virtually useless unless some technique such as a 'double blind' is used". With drugs of high effectiveness in the treatment of the disorder being investigated, the results are obvious from a comparison between treated and untreated patients. For example, a "double blind" technique was totally unnecessary to establish the effectiveness of penicillin, other antibiotics and sulphonamides against susceptible organisms. On the other hand, with drugs of comparatively low potency and incapable of producing dramatic effects, a "double blind" technique with careful statistical analysis is useful. "Tofranil" does, in many cases of depression, especially those seen as out-patients, belong to the former category: its effects are marked, often dramatic (see case histories, MacLean *et alii*[2]) and to a large extent predictable in time of onset.

The study by MacLean *et alii* was not "an uncontrolled trial". In a large majority of the cases, the patients acted as their own "vertical controls", in that their symptoms were of long duration and had been treated with a large variety of drugs without significant lasting improvement until "Tofranil" was used.

It is of interest to compare the results obtained by MacLean *et alii*[2] with those of Ball and Kiloh,[3] who used placebo tablets instead of Tofranil for a "randomized" half of their out-patients. Maclean *et alii* obtained an improvement rate of 73%. Ball and Kiloh reported: "In endogenous depression 74% of cases showed a good response to the drug, while 22% responded to the placebo."

The ethics of using a placebo instead of a preparation believed to be potent against a serious illness is very questionable. Ball and Kiloh mentioned a case that illustrates this: one patient committed suicide during the trial shortly after starting on the placebo.

It will be interesting to see what further knowledge concerning the effectiveness of "Tofranil" in depression Dr. Bartholomew elicits from his investigation, which he has indicated as similar to "a short-duration 'double blind' trial using small numbers".

Yours, etc.,

22 Fellows Street,
Kew, E.4,
Victoria.
April 7, 1960.

C. H. NOACK.

SIR: Dr. Allen Bartholomew's severe comments (MED. J. AUST., April 2, 1960, page 556) on the methodology so often employed, even nowadays, in medical research are scientifically inevitable. The aims of science are debatable; its necessities clear. Unless we all adhere to accepted conventions in scientific research, communication of our results becomes blurred, if not overwhelmed by semantic and pragmatic difficulty. In no area of medicine is this more apparent than in psychiatry.

We may adopt an idiographic or a nomothetic approach. If we adopt the former, our writings may be colourful and have much descriptive meaning for ourselves, but cannot easily be integrated into the body of scientific knowledge and must remain largely personal metaphysical speculation.

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[1] *Brit. med. J.*, 1959, 2:1052 (November 21).
[2] *J. ment. Sci.*, 1959, 105:1123.

[1] MED. J. AUST., 1960, 1:412 (March 12).
[2] MED. J. AUST., 1960, 1:414 (March 12).
[3] *Brit. med. J.*, 1959, 2:1052 (November 21).

The nomothetic approach, on the other hand, imposes considerable restrictions on our methodological discipline, but is more rewarding in the long run both for science and for the worker.

Stevens[1] has admirably summarized that scientific philosophy, based on "logical positivism" and on Bridgman's "operationism", which must form the basis of medical science in psychiatric research if these difficulties are to be avoided. Our observations must be recorded and communicated in such a way that they are able to be repeated under as nearly identical conditions as possible by other workers. Criteria must be defined "operationally"—i.e., against operations which are "public and repeatable". Of course, medical research requires much more than this (e.g., Woodger's[2] "bright ideas"); however, unless these basic requirements are met, the boundaries between science and metaphysics become indistinct.

In therapeutic trials, this is the more important where we aim to evaluate improvement in psychological status or mental symptomatology. Some of the independent variables which operate in such a situation (e.g., the natural history of illness to spontaneous remission, non-specific therapeutic "placebo" effects, etc.) are obvious; others (e.g., observer bias on the part of the experimenter or subject, sample inconsistency, etc.) less so. In such a trial our experimental group must be as precisely defined and as homogenous as possible. If we employ a control group, it must be matched against the experimental group for as many variables as we can conceive likely to affect the result. If we cannot use objective measures of change, we must state our criteria clearly—in a way which is "public and repeatable". We must guard against observer bias—a pragmatic difficulty inherent in subjective evaluations. We must gather our data in such a way that we can employ the yardstick of statistical probability against which to test our stated or implied hypotheses.

These and many others are the commonplace problems of medical research. It is clearly a difficult task to assess as "slightly improved, moderately improved, markedly improved or considerably improved" the various patients in a trial, remembering exactly their state before therapy, allowing for the tendency to spontaneous remission, avoiding any possible conscious or preconscious bias stemming from the experimenter's enthusiasm, or otherwise, of drug trials, his therapeutic orientation, etc., etc. Matched control groups, double-blind trials, sequential analysis, tests of statistical significance, etc., have no intrinsic merit, but are merely methodological manipulations aimed at dealing with some of the problems which exist (whether the worker recognizes them or not).

A glance through the medical journals of a few decades ago will disclose enthusiastic reports of drugs which we now accept as therapeutically valueless. These reports were written by authors of undoubted ability and integrity. It is obvious that scientific research requires more than these two qualities alone.

Yours, etc.,

I. PIERCE JAMES.

Perth,
Western Australia.
April 11, 1960.

HYPNOTISM AND SURGERY.

SIR: I have read with great interest the article on "Hypnotism and Surgery" (April 2, 1960) by a surgeon who himself uses this simple method of giving comfort to his patients without overloading them with dangerous drugs.

Mr. Susman writes a very clear account of the manner in which his attention was drawn to the value of hypnotism. Most medical practitioners use suggestion either wittingly or unwittingly, but too few recognize that deliberate suggestion under hypnosis can be so efficacious that in many cases drugs can be avoided, and yet the patient made comfortable, sedated and even rendered amnesic and analgesic thereby.

It should be emphasized that the patient must be a willing subject and have confidence in his doctor, and under these circumstances many patients can be helped by hypnotic suggestion with a minimum expenditure of time and effort. Even thirty minutes spent in inducing hypnosis is well worth while for any patient who is to undergo many subsequent painful procedures such as dressings of burns; if successful the first time, a specific suggestion can make future induction very quick and easy, and on the next occasion with that patient induction may take under five minutes, less than the time required to prepare and administer an intravenous injection.

Without wishing to make it appear that hypnotism is easy, nevertheless anyone who will take an intelligent interest in this subject, reading available literature and then relaxing his own inhibitions sufficiently to enable him to try it on appropriate patients, will soon meet with success, even though many attempts prove to be failures. Success is very convincing to the operator, and more successes will follow so that you now have a particularly valuable adjunct to your therapeutic armamentarium.

Like Mr. Susman, I agree that the risks are few, far less than those associated with drugs, provided that the practitioner confines its use to the immediate requirements.

Since the last war much greater interest has been taken in hypnotism than for many years, and there is now no lack of good books on this subject. In spite of this, there is still insufficient interest in our medical schools. It is time for us to grow up mentally and realize that hypnotism is not associated with magic and taboo.

Yours, etc.,

JOHN WOODLEY.

Director of Anæsthesia,
Launceston General Hospital,
Launceston, Tasmania.
April 12, 1960.

COMMERCIAL SAMPLES AND ADVERTISEMENTS.

SIR: Is there any way to stop commercial firms from sending me samples and advertisements? I retired from practice last year, but innumerable advertisements continue to be delivered at my old address. These are destroyed unread when readdressed to me. A great deal of money and energy is spent on the preparation and delivery and redelivery of these articles, and all to no purpose.

Those unwanted advertisements must be sent to many retired doctors, resulting in absolute denudation of forests to provide wood-pulp for paper for advertisements which are never read.

I can see that this wealth of advertisements will continue to pour in until I die. This happened to my predecessor, and I would like to know how to stop it from happening to me. Many other doctors must feel as I do, and commercial firms themselves would benefit if in any way they could be informed.

Yours, etc.,

PHYLLIS TEWSLEY.

10 Bradford Avenue,
Kew,
Victoria.
April 13, 1960.

CANCER.

SIR: Over a period of years I have endeavoured to take an intelligent interest in cancer, plus a little original thinking, and to me out of it comes, that it is most unfortunate that the term "cancer" has been applied to so many tumours whose biological behaviour is different.

Granted the human body has been described as a water bag, suspended on calcium sticks, I would go further and suggest that the bag contains millions of tubes, some large and others very small, with the result that blockage, leakage, or corrosion of these tubes go a long way to contribute to the many ills of man. Then, too, is not "man" a hormo-enzymatic individual? Were it not for him being such a tubo-enzymatic person, then cancer would become a local disease. Let me offer the opinion that the rudiments of life begin below the level of the cell.

But what of the contents of these tubes, which are carried to every living cell so that it may function? New growth itself is an adventure in both chemo- and biophysics, and as growth proceeds it is governed by the natural laws of mass, volume, cohesion and rotation, so that when a critical point is reached we get reproduction.

That reproduction (new growth) is influenced chemo- and bio-physically by local and remote control. The question then arises, does cancer occur as the result of the removal of these controls (one or both)? More so as

[1] "Psychology and the Science of Science", in "Psychological Theory", 1951, Macmillan, New York.

[2] "Physics, Psychology and Medicine", 1956, Cambridge University Press.

the cell is inherently dedicated to unlimited growth. I believe escape from normal control can occur, be it an accident local or remote—e.g. bacterial, hormonal, traumatic or enzymatic—or by the cell itself, which can become immune to the influence of these two factors.

Loss of control by either one or the other or both could quite easily cause mutative changes, in view of which it is not unreasonable to assume that cancer could be brought about by any of these changes taking place. Many of us who have been associated with malignancy over a period of years will have had the experience of a small local growth with a lung or liver riddled with secondary deposits, the local growth being kept under control by local cell action—these cells producing that unknown something. The secondaries removed from their local influences growing apace in their new environment; e.g., the cells of the breast may help to control the primary, but those of the lung or liver never.

Have these freed cells or cancer cells in general developed enzymes which have the power to disintegrate energy storing molecules of their host and bathe in a bath of molecules which activates and promotes their growth? Or does the body proper supply metabolites which produce the same effect?

In remote control, might I mention the part played by the endocrine glands in which the endocrine balance of the host is altered, and that growth can be controlled by appropriate hormones and by removing the glands which help to stimulate growth. This to me offers the big field of future research, rather than the direct kill of the cancer cells by drugs.

Surgery and physical therapy play their part if we do not delay. What of metastases? With a better understanding of the gene and the bio-physics of the life process, I feel that the ingenuity of man will overcome many of our problems of today. Perhaps a peep-hole already exists.

This, Mr. Editor, is a brief résumé of my observations and thinking. Yet I am old-fashioned enough to believe that much can still be learnt at the bedside.

Yours, etc.,

241 Oxford Street,
Bondi Junction,
New South Wales.
April 4, 1960.
KENNETH ADDISON.

THE DOCTOR AND HIS WAITING ROOM.

SIR: I got a bit of a shock myself the other day. An octogenarian patient said to me, "My word, I got a pleasant surprise in your waiting room just a while ago." I said, Why?" He said, "Well I've just read where Don Bradman is going to captain the Australian Eleven again."

Yours, etc.,

Padbury House,
170 St. George's Terrace,
Perth, W.A.
April 7, 1960.
J. M. O'DONNELL.

OBSERVATIONS OF THE USE OF "DARENTHIN", A NEW GANGLION-BLOCKING AGENT.

SIR: I was probably in error in describing "Darenthin" as a ganglion-blocking agent (MED. J. AUST., April 2, 1960). It would be better termed a sympathetic blocking agent.

Yours, etc.,

Wesley College,
University of Sydney,
Newtown, N.S.W.
April 6, 1960.
IAN MACKIE.

THE HEALTH OF IMMIGRANTS: SOME OBSERVATIONS FROM GENERAL PRACTICE.

SIR: In addition to Dr. J. M. Last's article in the January 30, 1960, issue, I would like to draw the profession's attention to tuberculosis in Greek migrants. From June, 1959, this practice has diagnosed three cases of primary pulmonary tuberculosis in children under the age of three, five cases of tuberculous pleural effusion in adults, all of whom were in their early thirties, and four other cases of pulmonary tuberculosis. It is important to note that all of these cases were in Greek migrants; there was not a single case in the Italian community, which forms a big part of this practice. I would like to take the opportunity of thanking Dr. Harris, the Director of Tuberculosis, Dr. F. Walton and Dr. M. Glick for their assistance in investigations of these cases. One wishes to thank particularly the Wollongong Hospital Chest Clinic, as were it not for this unit one would have a lot of difficulties with these cases.

Yours, etc.,

Cringila, N.S.W.
February 3, 1960.
L. M. LAVRIN.

THE PROBLEM OF INJURY AND ACCIDENT.

SIR: Dr. J. C. Fitzherbert, in the Journal of April 16, 1960, writes: " . . . an orthopædic surgeon for the bone injuries . . . ".

In planning the care of accident cases, it is essential to avoid such misconceptions on the function of the orthopædic surgeon. He treats a functional entity, soft parts as well as bones, and so to assist Dr. Fitzherbert and those who might think likewise I quote Sir Robert Jones, who defined orthopædic surgery as: "The treatment by manipulation, operation, re-education and rehabilitation of the injuries and diseases of the locomotor system." And Professor McMurray: "The simplest definition is that it is concerned with injury, deformity and disease of the limbs and spine."

Yours, etc.,

143 Macquarie Street,
Sydney.
April 19, 1960.
C. C. MCKELLAR.

DYSTONIC REACTION TO PERPHENAZINE ("TRILAFON").

SIR: I read with interest the article on "Dystonic Reaction to Perphenazine ('Trilafon')" by John Watson (MED. J. AUST., April 2, 1960).

A few days ago we had a woman suffering from an overdose of "Amytal". As she was depressed she received three five-milligramme doses of "Trilafon" intramuscularly at 12 hours' intervals. She developed very painful spasms of the jaw. She had no other signs. Ten millilitres of calcium gluconate was given intravenously without any effect. She responded, however, to 1·5 grains of "Pentobarbital" and a "codein co." tablet.

We had one other case who responded in a similar manner to "Trilafon".

Yours, etc.,

Senior Resident Medical Officer,
Sutherland Shire District Hospital,
Caringbah, N.S.W.
April 4, 1960.
EDITH ADLER.

Obituary.

GILBERT BROWN.

WE are indebted to SIR HENRY NEWLAND for the following account of the career of the late Dr. Gilbert Brown.

Dr. Gilbert Brown, who died on January 6, 1960, at the age of 77, was, as Sir Allen Daley has testified, a pioneer of modern anæsthesia in Australia. He was a Lancastrian, born at Wigan. He graduated M.B., Ch.B., from the University of Liverpool in 1908, winning the Robert Gee Prize in Diseases of Children in the final examination. At that time the Liverpool Medical School had a great name in the land, four outstanding men—Robert Jones, Ronald Ross, Charles Sherrington and F. T. Paul—having active association with it. For Paul, whose two-stage operation of colectomy had won him an international reputation early in the present century, Brown had especial personal regard. The following resident appointments at Liverpool were held in succession by Brown: ambulance surgeon, house surgeon

and house physician at the Liverpool Royal Infirmary; house surgeon at the Women's Hospital; house surgeon, house physician and senior resident medical officer at the Royal Liverpool Hospital for Sick Children.

After a short sojourn at sea as ship's surgeon, Gilbert Brown proceeded to South Australia in 1912. He practised first in Snowtown and then Gilberton. His medical practice was interrupted by the first World War. He was commissioned captain in the Australian Imperial Force and was posted senior resident medical officer, Woodman's Point Quarantine Station, Western Australia. He was about to embark for the front when peace was declared.

In 1920 he was appointed specialist anæsthetist to the section of plastic surgery for wounds of the face and jaws at Repatriation Hospital, Keswick. He soon proved himself a master of intratracheal technique. In addition to these part-time duties, he was appointed anæsthetist to the Adelaide Children's Hospital and a year later to the Royal Adelaide Hospital, where he also held the position of instructor in anæsthetics, a university appointment. The onerous duties of all these offices compelled him to confine his practice to that of anæsthetics.

The late twenties and early thirties were years of fulfilment. In 1929 he was elected president of the Section of Anæsthetics of the Australasian Medical Congress (B.M.A.) and was honoured overseas by his appointment as vice-president of the Section of Anæsthetics at the centenary meeting of the British Medical Association in London in 1932. He obtained the diploma of anæsthesia in 1935, and, not without honour in his old home town, was in the same year elected an honorary member of the Liverpool Anæsthetic Society.

He became a foundation Fellow of the Faculty of Anæsthetists of the Royal College of Surgeons of England in 1950, and subsequently a foundation Fellow of the Faculty of Anæsthetists of the Royal Australasian College of Surgeons. He was first president of the Australian Society of Anæsthetists, which he did so much to found.

In World War II he held the commission of major, and was attached to the 105th Australian Military Hospital as specialist anæsthetist, and was consulting anæsthetist to the Repatriation General Hospital at Springbank, South Australia.

Gilbert Brown was a regular attendant at the meetings of the South Australian Branch of the British Medical Association, and served on the Council in 1946-1947. His long and distinguished services to anæsthesia were recognized by the bestowal upon him of the C.B.E. in 1952. He was a J.P., and a rank he much valued was that of Officer of the Order of St. John of Jerusalem. He was married early in his career to Dr. Marie Simpson, who predeceased him.

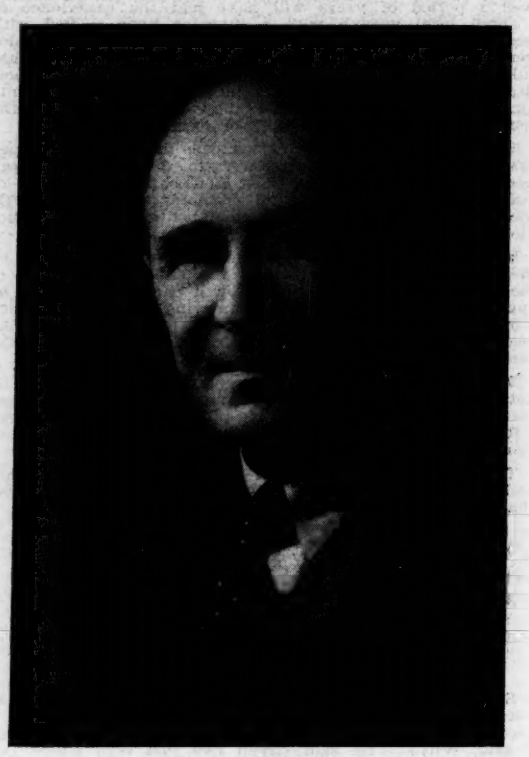
For 30 years, dating from the end of World War I, I enjoyed with Gilbert Brown friendship and intimate professional relations. During that long and happy period he gave anæsthetics at the Royal Adelaide Hospital, the Adelaide Children's Hospital and the Repatriation General Hospital and in my private practice. I now acknowledge the tranquillity that his skill vouchsafed to me. He never fussed and I never saw him flustered. What always impressed me was the infinite, constant and imperturbable care he took to eliminate the risks which in some degree attend anæsthesia in the pre-operative, operative and post-operative periods.

Gilbert Brown won the admiration of all who knew him by the quiet courage with which he bore the events—coronary thrombosis, prostatectomy, paralysis agitans—which shattered his health. The story of his life is a legacy of which his son may well be proud.

DR. G. R. TROUP writes: Time and generations pass so rapidly that it is easy to lose sight of the significant part that individuals have contributed during their lifetime when the end comes. Gilbert Brown was one whose influence on the many he taught will live on for years to come. He was the undisputed founder of modern anæsthesia in Australia, at a time when anyone with the temerity to emerge from the rag-and-bottle era was looked at askance. He realized early the value of keeping accurate anæsthetic records, and by his personal example instilled the essential habit into those with whom he came in contact. His work on the causation of anæsthetic deaths is well known and widely quoted. Again, he set the example to initiate committees of inquiry into anæsthetic deaths in centres where these could be of material benefit.

He was the main influence in the founding of the Australian Society of Anæsthetists in Hobart in 1936, and was its first president for some years. It was from this Society that the Faculty of Anæsthetists of the Royal Australasian College of Surgeons emerged. The influence of Brown of Adelaide on Australian anæsthesia during the last three decades has indeed been a profound one, and may not be fully appreciated by the younger graduates today.

His charm of manner, his humour (expresed in that soft voice that was never raised) and his kindness of heart to all, rounded off a personality that it was one of life's privileges to have known and fondly admired.



DR. H. J. DALY writes: It is a saddening yet wholesome thought to write of a friend who has passed out of our midst, and so I write of Gilbert Brown, to keep green the memory of one of our pioneer anæsthetists in Australia. He was born in Wigan, Lancashire, England, in 1883, and died on January 6, 1960, at Calvary Hospital, Adelaide, in the care of the Blue Nuns, who nursed him in his declining years with the kindness and care shown by those who devote their lives to the comfort and welfare of the sick and dying. He took his medical degrees at the University of Liverpool, and in 1912 came to settle in a triangular practice, as surgeon to the group, at Snowtown, some ninety miles from Adelaide.

In 1914, on the outbreak of World War I, Gilbert Brown carried on the general practice of all members of the partnership, and in 1918 was freed to enlist for overseas service. He embarked, but when he reached Durban, hostilities had ceased. In 1919, he and his wife came to practise at Gilberton, a suburb of Adelaide.

In his early post-graduate years, he showed an interest in anæsthetics by a paper published in *The Lancet* in 1911, entitled "Notes on Three Hundred Cases of General Anæsthesia Combined with Narcotics". He was stimulated to pursue this interest when he became associated with Mr. (later Sir Henry) Newland at the Repatriation Hospital, Keswick, Adelaide, a most cherished association and friendship, especially during the post-war years of World War I.

He held appointments at Adelaide Children's Hospital (1920 to 1929) and the Royal Adelaide Hospital (1921 to 1946) and was later made consultant anæsthetist to both these institutions. In addition, he was instructor in Anæsthetics to both medical and dental students at the University of Adelaide for some fourteen years.

In World War II, he served as anæsthetist at the Repatriation General Hospital, Heidelberg, with the rank of major. These activities he managed to combine with general practice, because anæsthetics as a specialty had not yet emerged. It can truly be said that he organized and led the way to progress in anæsthesia at all the centres in which he served.

He wrote many articles and papers to the journals on anæsthesia; too numerous to mention here, they are listed in the "Quarterly Cumulative Index Medicus".

A splendid tribute to Gilbert Brown by Geoffrey Kaye of Melbourne was published in 1950 in *The British Journal of Anæsthesia*, entitled "Brown of Adelaide'.

At the fourth session of the Australasian Medical Congress (B.M.A.), held in Hobart in 1934, those interested in anæsthesia met in the lounge of Hadley's Hotel, and the idea of forming the Australian Society of Anæsthetists was enthusiastically discussed and adopted. Gilbert Brown was elected the first president, and he successfully guided this Society in its early formative years.

He was granted the Diploma in Anæsthetics of the Royal Colleges of Physicians and Surgeons (England) in 1935, and soon after returned home, to become president of the Section of Anæsthetics of the British Medical Association, which honoured Australian members by holding its annual meeting in Melbourne in that year.

The C.B.E. bestowed on Gilbert Brown by Her Majesty the Queen in 1954 for his many contributions to anæsthesia was a well-merited and hard-earned reward to the first anæsthetist to be so honoured in Australia.

In appearance, Gilbert was a tall, well-built man, of ruddy complexion. He could be best described as a typical North of England country gentleman. He had a kindly manner and simple tastes, and was always well groomed, being meticulous in the care of his clothes, which were mostly tailored for him by Walker, of Albermarle Street, London—possibly his one extravagance. He was of a retiring disposition, and rather avoided speaking at our meetings; but when he felt it was time to join in, he would discourse at length, and what he said was always of great practical value. He always listened carefully to his friends and weighed every word said, occasionally nodding his head, muttering "Quite, Quite!", to assure the speaker he was taking it all in. He loved his pipe; it was his constant companion, and he liked to bite it and clamp it between his teeth or thrash imaginery ashes out of it, looking into the bowl which he must have known was empty, seeking thoughts before he spoke in reply.

Shortly after his election to the Fellowship of the Faculty of Anæsthetists of the Royal College of Surgeons he began to suffer from generalized atherosclerosis, and later from Parkinson's syndrome and finally cardio-vascular failure. I have before me part of a letter written when he was not feeling well, which shows his courage in the face of an illness which he must have known had only one outcome.

> Everyone says how well I look but I am still feeling doddery. However, I think that I am taking a slightly longer stride and hope to get out of low gear into second gear soon.
>
> I have had a letter from the Faculty of Anæsthetics of the Royal College of Surgeons that I have been elected a Fellow and am entitled to stick F.F.A.R.C.S. after my name. I do not want to do so particularly, but it is quite an honour. Probably, Geoffrey had something to do with it. [And then modestly, as in an aside to a friend] I am very glad to have it!

Vale, Gilbert Brown, good friend and companion! though you have passed on, we, your contemporaries, retain a vivid and warm memory of you.

CHARLES FRANCIS DREW.

We are indebted to Dr. R. L. Thorold Grant for the following account of the career of the late Dr. C. F. Drew.

Charles Francis Drew, who died on February 19, 1960 at Adelaide, was a member of an old South Australian family. His parents, Thomas and Catherine Drew, lived at Burra, where Charles was born in 1888. He went to school at Prince Alfred College, from there entering the University of Adelaide as a medical student; he subsequently graduated as M.B. and B.S. in 1911.

During his undergraduate days, he distinguished himself on the athletic side, representing his university in cricket, football and athletics, for each of which he was awarded a "blue", thus sharing with Gordon Campbell the distinction of becoming the first "triple blue" of the University of Adelaide. He also played League football with the North Adelaide team, and represented the State in football and cricket.

After graduation he went to Kadina, where he worked with Dr. Arthur Powell in a large country practice for eighteen months. His intention had then been to go to England for post-graduate work, but war was declared. He at once saw to it that his services were made available to his country. To avoid the delay entailed by a period of many months spent in camp in Australia, he went to England, where he joined the Royal Army Medical Corps in 1915. His war service was distinguished, and it was typical of the modesty of the man that this was known to few. He served in advance dressing stations in France for the whole period of the war, except for a spell of six months, which was spent in a base hospital. During this service in the line he was attached to Guards divisions, in turn with Scots, Grenadier and Coldstream Guards. He attained the rank of major; he was mentioned in dispatches in 1917, and he was awarded the Military Cross in 1918. In 1919 he was attached to the Army of Occupation, based at Cologne.

He returned to South Australia in 1920, and a year later he married Mollie, daughter of T. B. Gall, an Adelaide solicitor. In 1921 he acquired the practice of Dr. W. J. Gregerson, at Hindmarsh, and he worked in this large general practice in an industrial area for the rest of his life. Measured in terms of the affection, loyalty and respect of a large number of people, this was indeed a wealthy practice. His surrounding professional brethren all liked him immensely, which was an indication of his personality and his conception of medical ethics.

The South Australian Branch of the British Medical Association has reason to be grateful to Charles Drew for his services on the Council of that body. He served as a councillor from June, 1928, till June, 1930, and again from June, 1939, till June, 1942. Included in this service was a term as vice-president in 1941 and 1942. Attempts were made on several occasions to persuade him to accept nomination as president of the branch. He refused this honour, as he conducted a large practice single-handed and could not devote the required time to this office.

He found time for sport during his busy professional life. He played tennis and golf, and won the A.I.F. Golf Cup in 1928.

During the last war he conducted the practices of two of his associates in Hindmarsh who had gone on active service. This extra work, added to his own, was a strain on his health which he accepted uncomplainingly.

Charles Drew is survived by his wife and two sons, the younger of whom is a member of the medical profession. The death of this splendid man is deplored by all who knew him. His example of service to his country and to his profession will stand as his monument, as will the place he occupied in the hearts and homes of his patients.

FRANCIS GORDON ARCHER CEREXHE.

We are indebted to Dr. G. R. Faithfull for the following account of the career of the late Dr. F. G. A. Cerexhe.

Francis Gordon Archer Cerexhe was born at Wollstonecraft on April 17, 1916, the son of Francis Gordon Cerexhe and Essie Melissa Cerexhe (*née* Eagles). His father was an engineer, who had migrated from London to Australia at about the turn of the century, and his mother was a distant relative of Tyson "the cattle king". Unfortunately Gordon, as he was always known, lost his mother when he was only six years old, and so he and his father maintained a very close attachment. The two main interests in his life, medicine and engineering, manifested themselves early, but he decided to be a doctor with engineering as a hobby, and when he grew up he became a keen motor mechanic, servicing and repairing his own car when time permitted.

His schooldays were spent at Sydney Grammar School, where he acquired a reputation as a good rifle shot, and his reputation was maintained when he shot with the Sydney University Regiment on going up to the University. Photography and sailing were also hobbies, and he spent

a couple of his early years at the University living on his cruiser, the *Banyanda*. Gordon was a student at St. Vincent's Hospital, and in his year book he is described by a quotation from Burns as "plain plodding industry and sober worth".

After his graduation in 1945, he had a year's residency at Wagga Wagga Base Hospital, and then he went to England with his father for two years, where he worked in several hospitals. In 1952, after his return from the United Kingdom, he married Miss Betty Black, of Melbourne, and set up in practice at 60 Avoca Street, Randwick, where he was to stay for the remainder of his short life. The Eastern Suburbs Local Association of the British Medical Association was a particular interest, and he was a committee member and delegate to the quarterly meetings of Branch Council. He was also a divisional surgeon of the St. John Ambulance Brigade.

I had the privilege of attending many of Gordon Cerexhe's patients during his last illness, and it was very apparent from the esteem in which they held him that Gordon was friend as well as medical adviser to those families. Gordon's last few months of life were a lesson to us in bravery in the face of overwhelming odds. He died on January 19, 1960, leaving behind his wife, Betty, his father, and two sons (Andrew, aged six years, and Peter, aged four years), and a daughter (Carolyn, aged 19 months). He will be sadly missed by his patients and friends.

Notes and News.

Third Australasian Conference on Radiobiology.

The third Australasian Conference on Radiobiology will be held in the Department of Preventive Medicine, The University of Sydney, from August 15 to 18, 1960. Overseas visitors who will contribute papers to the programme are Dr. Peter Alexander (U.K.), Professor I. Berenblum (Israel), Dr. H. J. Curtis (U.S.A.), Dr. C. E. Ford (U.K.), Dr. Jacob Furth, (U.S.A.), Professor A. W. Galston (U.S.A.), Dr. D. A. G. Galton (U.K.), Dr. F. W. Gunz (N.Z.), Professor P. C. Koller (U.K.), Dr. Georges Mathe (France), Dr. B. R. Nebel (U.S.A.), Dr. Phan The Tran (Viet Nam), Dr. S. Rubenfeld, (U.S.A.) and Dr. J. Read (N.Z.). The subject matter of the main speakers will include: the biological mechanism of cell and tissue damage induced by radiation, comparison of the biological effects of radiation with radiomimetic chemicals and immediate and delayed effects of radiation (including the effect of radiation on the immune response; the stepwise development of the radiation injury at the cellular level, comparative biochemistry of radiomimetic chemicals and radiation, and chemical protection against radiation *in vivo* and *in vitro*; radiation-induced aging in mice, biological effects of cosmic rays, and delayed effects of radiation on seeds. Papers have also been received from contributors in the Universities of Tasmania, Melbourne, Sydney, and New South Wales, the Commonwealth Scientific and Industrial Research Organization and the Australian Atomic Energy Commission. The papers will cover the fields of biology, biochemistry, biophysics, genetics and immunology in relation to radiation.

The proceedings will be published by Butterworths. Authors will be sent notes for their guidance and are asked to follow the instructions given. Their cooperation in this way will be of great assistance and will expedite publication. Suggested titles and summaries will be accepted by the Convener until the end of April, 1960. Authors are reminded that the complete manuscript, double-spaced with one copy as well as the original, should be in the Convener's hands by June 30, 1960, for inclusion in the proceedings. The Convener is Dr. Peter Ilbery, Department of Preventive Medicine, University of Sydney, New South Wales.

Clinical Radiology: The Journal of the Faculty of Radiologists.

The Faculty of Radiologists in London has for some time now been publishing a journal under the title of *The Journal of the Faculty of Radiologists*. The publishers were John Wright and Sons, Limited, of Bristol. With the increasing circulation and the achievement of international status, a decision has been made to change the title and the journal has now appeared as *Clinical Radiology: The Journal of the Faculty of Radiologists*. The new publishers are E. and S. Livingstone, Limited, of Edinburgh and London. The first issue of the journal under its new title is Volume II, Number 1, January, 1960. It is made clear that the change of title implies no change in policy; this remains as before, the publication of scientific papers of interest to diagnostic radiologists and to radiotherapists, with the main emphasis on clinical radiology.

International Conference on Congenital Malformations.

The first International Conference on Congenital Malformations will be held in London from July 18 to 22, 1960, under the sponsorship of The National Foundation (U.S.A.). The Honorary Presidents of the conference are Mr. Basil O'Connor (U.S.A.) and Sir Geoffrey Marshall (England). The General Chairman is Professor J. D. Boyd (England). The Executive Secretary and Treasurer is Mr. Stanley E. Henwood (U.S.A.). The conference is to be divided into seven sessions devoted respectively to incidence, intrinsic factors (genetics), extrinsic factors (environment), general developmental mechanisms, abnormal developmental mechanisms, maternal fœtal interactions, physiological and medical problems, and perspectives. Correspondence should be directed to the Secretariat of the First International Conference on Congenital Malformations, 67 New Bond Street (Dering Yard), London, W.1, England.

Decrease in Cases of Typhus.

Cases of louse-borne typhus, which were counted in millions after the first World War, and in hundreds of thousands after the second, amounted to only 5800 in 1959, according to provisional notifications recorded in the latest issue of the *Weekly Epidemiological Record* of the World Health Organization. This represents a decrease of more than a thousand cases from the 1958 figure. The biggest drop was in Ethiopia, which also had the largest number of cases in both years, 4749 in 1958 and 3964 in 1959.

International Congress on Occupational Health.

The thirteenth International Congress on Occupational Health will be held at New York from July 25 to 29, 1960. The Congress is sponsored by the Permanent Committee and International Association on Occupational Health. Further information may be obtained from the office of the Federal Council of the B.M.A. in Australia, 135 Macquarie Street, Sydney.

"Glossary of Dietetic Terms."

The Nutrition Section of the Australian Institute of Anatomy, Canberra (Commonwealth Department of Health) has issued a booklet entitled "Glossary of Dietetic Terms", which has been planned for the information of those concerned in any way with special diets. At the moment it is available as a separate issue, but it is expected in the future to be incorporated in the publication "Notes on Special Diets for Use in Hospitals". The glossary is available on request.

The Royal Melbourne Hospital Clinical Reports.

We have received the latest two issues of the *Royal Melbourne Hospital Clinical Reports*, dated March and September, 1959. The March issue contains Part I of an article on acute infections of the hand, by John Wright Smith, and papers by C. Bridges Webb on shock in myocardial infarction and by E. S. R. Hughes on restorative excision of tumours of the rectum. The September issue contains some observations on extradural hæmorrhage by Reginald Hooper and a report by M. J. Etheridge and Kevin Catt of a case of phæochromocytoma as well as Part II of John Wright Smith's article on acute infections of the hand.

The Japanese Journal of Gastroenterology.

The Gastroenterological Society of Japan has been publishing a journal in Japanese for some fifty years. Now, however, it has decided to publish an English edition of this journal, and the first number consists of the proceedings of the forty-fourth annual meeting of the Society held in 1958. The Society hopes that the English edition will enhance international relations and serve as an introduction for Japanese research work in the field of gastroenterology. The journal is to be issued once a year for a subscription of five dollars.

Post-Graduate Work.

SURGICAL SEMINAR AT ST. VINCENT'S HOSPITAL, SYDNEY.

A SURGICAL SEMINAR will be held in the Students' Lecture Theatre, fifth floor, St. Vincent's Hospital, Sydney, on Monday, May 2, 1960, at 5.15 p.m. Mr. N. C. Newton will speak on "Carcinoma of the Larynx". All medical practitioners are invited to be present.

THE CARDIAC SOCIETY OF AUSTRALIA AND NEW ZEALAND.

THE Cardiac Society of Australia and New Zealand announces that Dr. Wallace Brigden, M.A., M.D., F.R.C.P., physician, of the London Hospital and the National Heart Hospital, London, will attend and take part in the discussion of a series of case presentations, to be held at the Maitland Lecture Theatre, Sydney Hospital, on Monday, May 23, 1960. The programme is as follows: 10 a.m., "Surgical Aspects of Cardiology"; 11.30 a.m., "Medical Problems in Cardiology: I"; 2.30 p.m., "Medical Problems in Cardiology: II"; 4 p.m., "Electrocardiography".

All medical practitioners are invited to attend.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE following additions and amendments have been made to the Register of Medical Practitioners for New South Wales, in accordance with the provisions of the *Medical Practitioners Act*, 1938-1958.

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (1) (a) of the Act (qualifications being M.B., B.S., 1960 (Univ. Sydney) unless otherwise stated): Abramovich, David Rheuben; Allen, Keith Muree; Ambrose, Grahame Aubrey; Anastas, Nicholas Constantine; Angus, Ian Stuart; Apted, Douglas Frank; Armstrong, Michael Lawrence; Arter, Warren James; Baggott, John Bernard; Baral, Jacob; Barnes, Doris Elizabeth; Barold, Samuel Serge; Basset, Heather Marjorie; Beard, David Harry; Bennett, Melvyn Douglas; Best, Trevor Norman; Birrell, Warwick Robert Sinclair; Bishop, Janice Margaret; Blum, Peter William; Borman, Helen; Bridger, George Patrick; Carney, Donald Earl; Carroll, Raymond Leon; Casey, Brian Hal; Casey, Kerry Vincent; Celermajer, John Marian; Chalker, Adrian Kenneth; Chambers, Helen Jennifer; Chapman, Barry Lloyd; Chapman, John Clarence; Cheung, Yee-Tim Joseph; Cho, Kai Shing; Chung, Robert Milton; Clubb, John Stafford; Conrad, Peter; Cooke, David Edmund; Cooper, Raymond John; Corry, John Richard; Coyle, Patricia Margaret; Crighton, Colin Anthony; Cull, Donald Brett; Darcy, Leslie Osborn; Davey, Martin Geoffrey; Davis, Colin George; Davis, John Mark; Drake, Richard Geoffrey; Dyball, Kenneth Henry; Edmonds, Carl Wildred; Emmett, Arthur John; Evans, Ian Edward Hepburn; Failes, Beryl Margaret; Farnsworth, Robert Housley; Farrer, Paul Andrew; Ferguson, Andrew Stewart; Foo, Jennifer Kim Geok; Foote, Alison Mavis; Frankland, Howard Edward; Gerakiteys, James; Glen-Doepel, Josephine Alice; Goldman, Peter; Gordon, Raymond Warwick; Gordon, Robert Gabriel; Gray, William Charles; Grierson, Jean Margaret; Hammill, Garry Leslie; Hammill, Helen Muriel de Carteret; Han, Lap Kwong; Harrington, John Francis; Harris, Philip Geoffrey; Heppell, Robert Rutherford; Hew, Joseph Weng Onn; Higgins, Shirley Grace; Higgins, Vincent William; Howard, Ronald George; Jackson, Donald Warren; Jervie, Ann Elizabeth; Johnson, Graeme Warwick William; Kald, Malle; Kearney, Brian Edmund; Kern, Ian Barry; Kovacs, Stephen George; Lalak, Ivan John; Lane, Arthur Oleg; Lawrence, Ronald; Lecky, Jocelyn Olive Helen; Lim, Boon-Keng; Lo, David; Logan, John Wride; Long, Peter Anthony; Lord, Reginald Sidney Albert; Low, Peter Eng Wah; McClatchie, Gordon De Siou; McGarry, Desmond Joseph; McKillop, Robert Graham; McLean, Alan Gordon; Mah, Alban; Martin, Michael David; Mead, Margaret

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED MARCH 26, 1960.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	2(2)	1	..	..	..	..	..	3
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	3	..	..	..	..	..	3	..	6
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	1	..	..	..	..	..	..	1
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	6(1)	12(10)	2(1)	..	..	..	6	1	27
Diphtheria	..	..	..	..	..	..	..	..	..
Dysentery (Bacillary)	..	..	3(2)	..	1(1)	..	1	..	5
Encephalitis	..	..	..	..	..	..	1	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	1	1(1)	..	..	2
Infective Hepatitis	41(10)	30(23)	13(4)	4(3)	1(1)	..	..	1	90
Lead Poisoning	..	..	1	..	..	..	..	..	1
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	3	..	..	..	..	..	3
Malaria	..	..	2(1)	..	..	..	1	..	3
Meningococcal Infection	..	3(2)	..	..	..	..	1	..	4
Ophthalmia	..	..	..	..	6(6)	..	..	..	6
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	1	..	..	..	..	..	..	..	1
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	12(7)	..	1	2(2)	..	..	1	16
Salmonella Infection	..	..	..	..	3(3)	..	..	..	3
Scarlet Fever	4(2)	22(18)	2(1)	2(2)	..	..	..	..	30
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	1(1)	..	..	..	..	..	1
Trachoma	..	..	..	..	..	..	20	..	20
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	25(19)	21(22)	15(3)	5(4)	9(9)	2	2	..	89
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Mary; Miles, Neil MacKay; Miller, Geoffrey Gordon; Miller, Jacqueline; Millist, Warren Henry Russell; Morgan, Trefor Owen; Murphy, Anthony Hilary; Naughton, Michael Anthony Patrick; Nelson, David Selwyn; Nelson-Marshall, Malcolm Gifford; North, Robert Alan; O'Brien, John Patrick; Oldfield, Allen Stanley; O'Reilly, Richard Francis; O'Rourke, Michael Francis; O'Sullivan, Dudley Joseph; O Sullivan, Gabrielle Irene Maeve; Paingakulam, Joseph Anthony; Paszkowski, Janusz Kazimierz; Penny, Ronald; Phoon, Kenneth Wai Shing; Phoon, Mark Wai Tai; Pilgrim, Margaret Josephine; Plunkett, Edward Henry; Rae, Leslie Clyde; Revai, Eli Immanuel Reuben; Rundle, Robert Charles; Saareste, Ain Gunnar; Sachs, Martin; Scott, Ronald Daikeith; Sharah, Alexander Anthony; Sheldon, Donald Mervyn; Simpson, Edward James; Sinnett, Peter Frank; Smith, Robert Henry; Solomon, John Douglas; Southwell, Philip Brinsmead; Stening, Stephen Graham; Stephen, Robert Longfield; Stevens, Susan Margaret Borradaile; Stokes, Gordon Stewart; Swynny, Colleen Lessley Allein; Tancred, Patrick John; Tedder, Elizabeth; Tester, Malcolm Percy; Thompson, Patrick; Thompson, Philip Geoffrey; Thomson, Brian Ferguson; Tindal, Donald Stuart; Toohey, John Joseph; Truskett, Ian Douglas; Turtle, John Ross; Vakkur, George Juri; Walker, Thomas David; Walker-Smith, John Angus; Wallis, Denise Joan; Warden, John Charles; Weisberg, Edith; Wells, John Vivian; White, Gordon Ernest Middleton; Wickham, Joan; Wilson, John David; Chunn, Jeremiah Alfred, M.B., Ch.B., 1948 (Univ. New Zealand); Clarke, Mary Joan, M.B., B.S., 1958 (Univ. Queensland); Cox, Roslyn Woodrow, M.B., Ch.B., 1949 (Univ. New Zealand); Hamilton, David Wyndham, M.B., B.S., 1959 (Univ. Adelaide); Hodgson, Richard Berkeley, M.B., B.S., 1959 (Univ. Adelaide); Morris, Neville Johnston, M.B., B.S., 1959 (Univ. Adelaide) (Requirements of section 17 (3) to be satisfied); Page, Leland Ivor, M.B., B.S., 1953 (Univ. Adelaide).

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (1) (b) of the Act: Fogarty, Patrick Ambrose, M.B., B.S., 1958 (Univ. London); McFarlane, Violet Mary Milner, M.B., Ch.B., 1937 (Univ. Glasgow); Reitsma, Lucian Alan, M.R.C.S. (England), L.R.C.P. (London), 1951, D.A., R.C.P. & S., 1958; Shirreffs, Gordon Chisholm, M.B., Ch.B., 1957 (Univ. Aberdeen); Wilson, Alexander Scott, M.R.C.S. (England), L.R.C.P. (London), 1956; Wyatt, Walter, M.B., Ch.B., 1924 (Univ. Edinburgh), D.P.M. (London), 1927.

The undermentioned has been issued with a licence under Section 21A of the Act: Kanarek, Maksymilian, Urbenville-Woodenbong, for one year from March 25, 1960.

Nominations and Elections.

The undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Gerlach, Helmut Rudolf, M.D., 1923 (Univ. Breslau) (licensed under Section 21A of the *Medical Practitioners Act*, 1938-1958), Ivanhoe, New South Wales.

Faithfull, Donald Kingsley, M.B., B.S., 1959 (Univ. Sydney), 8 Milford Street, Randwick.

Coupland, William Warwick, M.B., B.S., 1959 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association: Baral, Jacob, M.B., B.S., 1960 (Univ. Sydney); Beard, David Harry, M.B., B.S., 1960 (Univ. Sydney); McLean, Alan Gordon, M.B., B.S., 1960 (Univ. Sydney); Tedder, Elizabeth, M.B., B.S., 1960 (Univ. Sydney); Johnson, Lindsay Albert, M.B., B.S., 1959 (Univ. Sydney); Pryor, Donald Sidney, M.B., B.S., 1959 (Univ. Sydney); Pallas, David Russell, M.B., B.Ch., 1954 (Univ. Wales), B.Sc., 1951 (Univ. Cardiff); Tarlington, Michael John Kevin, M.B., B.S., 1956 (Univ. Sydney); Mulvey, Peter Maxwell, M.B., B.S., 1957 (Univ. Sydney); Rugless, Kenneth Robert, M.B., B.S., 1957 (Univ. Sydney); Stewart, Peter William, M.B., B.S., 1957 (Univ. Sydney); Narkowicz, Stefan, M.D., 1937 (Univ. Wilno), regional registration, Section 21A of the *Medical Practitioners Act*, 1938-1958; Peukert, Joseph, M.D., 1944 (Univ. Prague) (licensed under the provisions of Section 21C (4) of the *Medical Practitioners Act*, 1938-1958; Ropicki, Lydia Irena, M.D., 1934 (Univ. Graz) licensed under the provisions of Section 21C of the *Medical Practitioners Act*, 1938-1958; Selecki, Borys Romuald, M.D., 1951 (Univ. Wroctaw) licensed on November 4, 1959, to do P.G. Research.

Deaths.

The following deaths have been announced:

Thomas.—Ivor Gwynne Thomas, on April 14, 1960, at Campbelltown.

Goldacre.—Peter Lionel Goldacre, on April 16, 1960, at Canberra.

Lloyd-Jones.—Raymond Lloyd-Jones, on April 16, 1960, at Goulburn.

Potts.—Keith Faulkner, on April 17, 1960, at Arncliffe, New South Wales.

Diary for the Month.

May 3.—New South Wales Branch, B.M.A.: Organization and Science Committee.

May 4.—Western Australian Branch, B.M.A.: Branch Council.

May 5.—South Australian Branch, B.M.A.: Council Meeting.

May 10.—New South Wales Branch, B.M.A.: Executive and Finance Committee.

Medical Appointments: Important Notice.

Medical practitioners are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

All articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

Authors of papers are asked to state for inclusion in the title their principal qualifications as well as their relevant appointment and/or the unit, hospital or department from which the paper comes.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to The Medical Journal of Australia alone, unless the contrary is stated.

All communications should be addressed to the Editor, The Medical Journal of Australia, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

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